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FDA's Contradictory Decisions Related to the Delaney Clause

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## Abstract

This paper will focus on FDA regulation under the Delaney Clause, and particularly regulations that have led to contradictory results. It first will examine the history and basic requirements of the Delaney Clause. It next will discuss cancer: statistics regarding the frequency, types, and causes of cancer. Then it will examine some foods and food additives that have been associated with some level of carcinogenicity and how FDA has handled them. It will conclude by discussing the inherent problems that the Delaney Clause presents in establishing a uniform system of regulation and, finally, by proposing some potential alternative ways in which FDA might better use its power to help the public avoid excessive exposure to carcinogenic food substances.

The Delaney Clause has been a source of controversy since its enactment in 1958. This paper first will chronicle the history of the Clause, and of FDA regulation under the Clause, and then will examine some of the contradictory decisions in regulation that the Delaney Clause has led FDA to make. It will focus on some of the contradictory decisions stemming from the Clause as applied to food additives, both among themselves and in opposition to natural, whole foods. This paper will be limited to the regulation of specific additives and will not address the (albeit quite important) issues of contaminated foods fed to animals, color additives, or pesticides.

## I. The Delaney Clause

The Delaney Clause, a 1958 amendment to the Federal Food, Drug, and Cosmetic Act of 1938, states that “the Secretary of the Food and Drug Administration shall not approve for use in food any chemical additive found to induce cancer in man, or, after tests, found to induce cancer in animals.”<sup>1</sup> Congress considered the addition of the Clause to the Act to be necessary out of fear that, without it, the public regularly would encounter carcinogens in their foods.<sup>2</sup>

### A. History

In the 1940s, relatively early in the history of FDA regulation, and well before the enactment of the Delaney Clause, the agency established a rule for potentially toxic, though not carcinogenic, substances: the safe human dose of a substance was considered to be 1/100 of the highest dose that caused no toxic effects in laboratory test animals (a

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<sup>1</sup> 21 U.S.C. § 348(c)(3)(A).

<sup>2</sup> Al Meyerhoff, *The Delaney Clause: Point/Counterpoint*, 19 EPA J. 42, 42 (1993).

level that now is known as the “no observed adverse effect level” (NOAEL)).<sup>3</sup> Such a safety factor, or level of tolerance, however, was never considered to be permissible among carcinogenic (or potentially carcinogenic) substances.<sup>4</sup> For these substances, FDA always has used a no-tolerance method of regulation; the agency banned two coal-tar colors that were known to be potentially carcinogenic in the 1940s as well as two artificial sweeteners and natural tonka beans and coumarin, a constituent of the tonka beans, in the 1950s.<sup>5</sup>

The first drafts of the Food Additives Amendment did not contain any version of the Delaney Clause.<sup>6</sup> In 1957, Congressman James Delaney revised his bill with the Clause’s first articulation: “The Secretary shall not approve for use in food any chemical additive found to induce cancer in man, or, after tests, found to induce cancer in animals.”<sup>7</sup>

On July 23, 1957, the Secretary of the United States Department of Health, Education, and Welfare (HEW) noted his objection to the Delaney Clause in a letter, stating that the Clause was not necessary; he noted that, if a food additive were found to cause cancer at the rate at which it was normally used, it would be declared unsafe by other means and, thus, be banned from the food supply without what he considered the unnecessary addition of the Delaney Clause.<sup>8</sup> The Secretary went on to assert that the Clause was overly broad in that it did not require food additives to be tested in the way that they would normally be used; he noted that “[s]cientists . . . can produce cancer in test

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<sup>3</sup> PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, *FOOD AND DRUG LAW* 1120 (2007).

<sup>4</sup> *Id.* at 1121.

<sup>5</sup> 15 Fed. Reg. 321 (1950); 19 Fed. Reg. 1239 (1954).

<sup>6</sup> Frederick H. Degnan, Esq. and W. Gary Flamm, Ph.D., *Living with and Reforming the Delaney Clause*, 50 *FOOD & DRUG L.J.* 235, 237 (1995).

<sup>7</sup> H.R. 7798, 85<sup>th</sup> Cong., 1<sup>st</sup> Sess. (1957).

<sup>8</sup> *Food Additives, Hearings Before a Subcomm. of the House Comm. on Interstate and Foreign Commerce*, 85<sup>th</sup> Cong., 1<sup>st</sup> and 2<sup>d</sup> Sess. 171 (1958).

animals by injecting sugar in a certain manner, and they can produce cancers by injections into test animals of cottonseed oil, olive oil, or tannic acid (a component of many foods).”<sup>9</sup> He also noted the potential absurd consequences, if the Delaney Clause were strictly enforced, of “rul[ing] out of the food supply sugar, vegetable oils, or common table beverages simply because, by an extraordinary method of application never encountered at the dining table, it is possible to induce cancer by injecting the substances into the muscles of test animals.”<sup>10</sup>

In 1958, a new food additives bill was reported out of committee without the inclusion of an anti-carcinogen clause.<sup>11</sup> After the bill was filed, Congressman Delaney argued for the inclusion of such a clause.<sup>12</sup> The Assistant HEW Secretary Elliot Richardson reiterated in a letter that the Clause was unnecessary; however, he stated that he would not object to a revised bill providing for appropriate tests.<sup>13</sup> In 1960, Congress included the Delaney Clause in the listing provisions of the Color Additives Amendments.

The Delaney Clause now appears in three separate parts of the Federal Food, Drugs, and Cosmetic Act of 1938: § 409 on food additives,<sup>14</sup> § 512 on animal drugs in meat and poultry,<sup>15</sup> and § 721 on color additives.<sup>16</sup> The prohibition in § 409 originally applied to pesticide residues as well; however, the Food Quality Protection Act of 1996 removed pesticide use from the prohibitive regulations of the Delaney Clause. The primary focus of this paper will be on the Delaney Clause as applied to food additives,

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<sup>9</sup> *Id.*

<sup>10</sup> *Id.*

<sup>11</sup> H.R. 13,254, 85th Cong., 2d Sess. (1958).

<sup>12</sup> *Living with and Reforming the Delaney Clause*, *supra* note 6, at 237.

<sup>13</sup> 104 Cong. Rec. 17,415 (Aug. 15, 1958).

<sup>14</sup> 21 U.S.C. § 348 (1982).

<sup>15</sup> 21 U.S.C. § 360(b) (1982).

<sup>16</sup> 21 U.S.C. § 376 (1982).

without examination of pesticide use. In particular, it will examine the contradictory results of applying it to food additives when carcinogenic substances naturally present in foods, or that form in ways such that they are not affirmatively added by human processes, are not so regulated.

## B. Controversiality

The Delaney Clause is notoriously controversial, due to its potential for overreaching and even (according to some with staunchly pro-regulatory views) for underreaching as well as its numerous uncertainties regarding term definitions and how properly to apply the Clause to the wide variety of food additives currently used. In 1958, when the Delaney Clause was first adopted, only four substances were known to cause cancer in humans: soot, radiation, tobacco smoke, and beta-naphthylamine.<sup>17</sup> By the 1970s, however, new scientific technology rendered determination of carcinogenicity much more sensitive, having increased between two and five orders of magnitude between the years 1958 and 1978.<sup>18</sup> Carcinogens were, by the 1980s, detectable at the parts-per-trillion level, up to a million times more sensitive than the rate at which they could be detected in 1958.<sup>19</sup> Currently, the world is significantly different than it was in 1958, and ability to detect small potentiality for carcinogenicity in foods continues to increase; some (albeit often infinitesimally small) potential carcinogenic effect is detectable in a hugely significant number of foods and food additives.

### 1. Quantitative risk assessment

Thus, to make the Delaney Clause possible to implement, FDA adopted a quantitative risk assessment method to evaluate such carcinogenicity. Rather than

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<sup>17</sup> 51 Fed. Reg. 28331, 28343 (1986).

<sup>18</sup> *Id.*

<sup>19</sup> *Id.*

banning a substance with a truly infinitesimal possibility of being carcinogenic, for FDA to declare a substance to be unsafe under the Delaney Clause, the substance must result in a risk to humans of more than one in one million of developing cancer over one's lifetime.<sup>20</sup>

Quantitative risk assessment first was used only to regulate carcinogenic animal drugs; however, by 1980, FDA had begun using the method of quantitative risk assessment to determine the potential carcinogenicity of constituents in food, drugs, and medical devices, as well as cosmetics.<sup>21</sup> Color additives are subject to stricter regulation than are most food additives, however: any risk of cancer in animals, even as small a risk to humans as one in nineteen billion over a person's lifetime, renders color additives unsafe under FDA standards.<sup>22</sup>

Quantitative risk assessment, though ostensibly preventing overregulation (at least to an extent) of food additives with real though negligent carcinogenic potential, did not come without its own problems and controversiality. The method involves "the mathematical extrapolation from high-dose laboratory animal data to derive estimates of the cancer risk associated with much lower human exposures from the consumer products."<sup>23</sup>

The uncertainties in the process of quantitative risk assessment render it necessary to make certain assumptions, which regulators normally do in the most conservative manner that is appropriate to avoid underestimating the risk of a substance's potential

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<sup>20</sup> D. Feinberg, *A Cookbook for a Consistent Food Safety Standard for Carcinogenic Foods: Looking to the Ingredients of a Food Rather Than Its Recipe*, 5 J. PHARMACY & L. 67, 76 (1995).

<sup>21</sup> FOOD AND DRUG LAW, *supra* note 3, at 1139.

<sup>22</sup> Public Citizen v. Young, 831 F.2d 1108 (D.C. Cir. 1987)

<sup>23</sup> FOOD AND DRUG LAW, *supra* note 3, at 1139.



carcinogenicity to humans.<sup>24</sup> Therefore, regulators generally assume laboratory animals to be appropriate models for determining risk to humans, use data from the most sensitive sex of the most sensitive species for testing purposes, consider benign tumors to be malignant for purposes of evaluation, and assume the relationship between dose of a food additive and physiological response of the treated laboratory animals to be linear (rather than having the response to the initial dose be greater than the response of additional amounts, leading to a curved response, a response that often is true in reality).<sup>25</sup> Thus, quantitative risk assessment leads to worst-case estimates in many cases, providing data that may overestimate a food additive's carcinogenic potential by several orders of magnitude.<sup>26</sup>

## 2. GRAS exception

The Food, Drug, and Cosmetic Act provides further complicates the Delaney Clause with its GRAS (generally recognized as safe) exception. The Act defines a “food additive” as

any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been

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<sup>24</sup> *Id.*

<sup>25</sup> *Id.*

<sup>26</sup> *Id.*

adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include ... (4) any substance used in accordance with a sanction or approval granted prior to the enactment of this paragraph 4 pursuant to this Act, the Poultry Products Inspection Act ... or the Meat Inspection Act of March 4, 1907....<sup>27</sup>

Therefore, products that were in use prior to 1958 generally are subject to less strict regulation, leading some people to accuse the Delaney Clause, and even the entire Food, Drug, and Cosmetic Act, as unfairly penalizing new substances over those that have been eaten for many years in the past.<sup>28</sup>

As noted above, a substance may be declared GRAS either through scientific procedures or through experience based on common use in food prior to 1958. To establish safety through scientific procedures requires the same amount (both quantitative and qualitative) of scientific evidence that would be required for the substance's approval as a food additive and ordinarily if the approval were to be based upon published studies, which may be substantiated by unpublished studies as well as by other data and information.<sup>29</sup> For a substance to obtain GRAS status through experience based on

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<sup>27</sup> 21 U.S.C. § 321(s).

<sup>28</sup> See, e.g., *A Cookbook for a Consistent Food Safety Standard*, *supra* note 20, at 78.

<sup>29</sup> *Guidance for Industry: Frequently Asked Questions About GRAS*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/ucm061846.htm> (last visited April 2011).

common use in foods, there must be a “substantial history of consumption for food use by a significant number of consumers.”<sup>30</sup>

### 3. De minimis exception

Because of the current potential for detecting miniscule amounts of possible carcinogenicity of so many commonly-consumed foods, FDA has adopted something akin to a *de minimis* exception in applying the Delaney Clause. The policy was necessary to prevent bringing thousands of foods under Delaney Clause regulation because of the high numbers of commonly-eaten foods that do have a trace amount of a known carcinogenic substance present either naturally or because of an unavoidable processing step.<sup>31</sup>

#### C. What qualifies as GRAS

As mentioned, a substance that is declared to be generally recognized as safe (“GRAS”) is exempt from regulation under the Delaney Clause. To qualify as GRAS, as noted, a substance must be shown to have had a substantial history of consumption by a significant number of consumers in the United States.<sup>32</sup> The substance must be safe in its intended use (prohibiting, therefore, GRAS status for all uses of a product that may be safe only for a limited or specific use).<sup>33</sup>

The GRAS exception, similar to the Delaney Clause itself, has been accused of favoring old, established substances over newer ones, and even favoring established uses of some particular substance over a new use for the same substance. Such favor is

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<sup>30</sup> *Id.*

<sup>31</sup> *A Cookbook for a Consistent Food Safety Standard*, *supra* note 20, at 79.

<sup>32</sup> 41 Fed. Reg. 53600 (1976).

<sup>33</sup> *United States v. An Article of Food*, 752 F.2d 11 (1st Cir. 1985) (in which the court held that, though nitrates naturally are present in vegetables and have been used to cure meat for much time, potassium nitrate could not be considered GRAS when used in drinks).

asserted even though a substance may have its GRAS status revoked if evidence casts doubt on its safety,<sup>34</sup> primarily because of how unlikely it is that FDA will revoke a commonly-consumed product's GRAS status.<sup>35</sup>

FDA officially refuses to recognize any known carcinogenic substance as GRAS.<sup>36</sup> However, because many natural foods are recognized as carcinogenic to some degree, FDA makes an exception (similar to the *de minimis* exception to the Delaney Clause) and permits a natural substance to remain GRAS even if it contains substances found to cause cancer in test animals even though a substance that itself is carcinogenic is forbidden from maintaining its GRAS status.<sup>37</sup>

#### D. What qualifies as added

If a substance is determined to be added, the manufacturer has the burden of proof regarding its safety; if a substance, on the other hand, is an actual food, however, FDA has the burden of proving its harmfulness.<sup>38</sup> Because the Food, Drug, and Cosmetic Act does not define “added substance,” determining its meaning has been left to FDA and the courts, who have come up with two distinct standards. The inherency standard declares all substances that are not inherent in the natural state of a food to be added.<sup>39</sup> The agency theory, however, considers a substance to be added only if at least a small amount is present because of human intervention.<sup>40</sup> The standard that FDA officially recognizes is the inherency standard.<sup>41</sup>

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<sup>34</sup> 41 Fed. Reg. 53600.

<sup>35</sup> See *A Cookbook for a Consistent Food Safety Standard*, *supra* note 20, at 80.

<sup>36</sup> See, e.g., 34 Fed. Reg. 17063 (1969) (FDA's decision to remove cyclamate from its GRAS list after learning of evidence of its carcinogenicity).

<sup>37</sup> *A Cookbook for a Consistent Food Safety Standard*, *supra* note 20, at 81.

<sup>38</sup> See, e.g., *United States v. Lexington Mill & Elevator Co.*, 323 U.S. 399, 411 (1914).

<sup>39</sup> See, e.g., *United States v. Boston Farm Center, Inc.*, 590 F.2d 149 (5th Cir. 1979).

<sup>40</sup> See, e.g., *Continental Seafoods, Inc. v. Schweiker*, 674 F.2d 38, 43 (D.C. Cir. 1982).

<sup>41</sup> *A Cookbook for a Consistent Food Safety Standard*, *supra* note 20, at 81.

Though the difference between the two standards initially may seem trivial, under certain situations, applying each standard to a substance would yield a far different result for purposes of FDA regulation. Certain substances, for example, such as aflatoxins in peanuts and corn are neither inherent in the natural state of the food nor added by human intervention; instead, aflatoxins result from mold growing on the foods.<sup>42</sup> If these aflatoxins are considered added substances, they will be regulated under the harsher “may render injurious” standard; if, however, they are not considered to be added, their regulation merely will be under the “ordinarily injurious” standard.<sup>43</sup> If the agency theory were to be applied, the aflatoxins would not be considered added substances; however, FDA’s inherency standard causes them to be considered added. Thus, under FDA’s inherency standard, peanuts with aflatoxins, not present in the peanuts’ natural state yet not present due to human intervention, are subject to harsher regulation by FDA than are foods whose harmful, or potentially carcinogenic, characteristics are inherent in their natural states.

E. Remaining problems

1. What is a carcinogen

Determining carcinogenicity would seem to be rather straightforward: any substance that is directly involved in causing cancer (one would think) should, under the common understanding of the term, be deemed a carcinogen.

Determining carcinogenicity for purposes of the Delaney Clause prohibitions, however, actually is a highly complex process. The Clause itself is notoriously silent on which substances should be classified as carcinogens. Applying the sweepingly broad

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<sup>42</sup> *Id.*

<sup>43</sup> *Id.*

definition mentioned above is nearly impossible, or at least would be highly problematic, because the current scientific technology renders it difficult not to detect at least a small possibility of carcinogenicity in almost any given food.<sup>44</sup> The most sensible way to distinguish those products that should be deemed carcinogenic under the Delaney Clause is to require them to pass a certain threshold either of the magnitude of potential harm they could cause or of their likelihood to cause such harm.

Just how potent a carcinogen a substance must be, or how likely to cause cancer the substance must be, to be classified as a carcinogen for Delaney Clause purposes is not the only problem. Even after determining what qualifies as a carcinogen (i.e., setting the standards) is settled, there remains the issue of accuracy of determining what qualifies (i.e., which products meet the previously-determined standards). The nature of the Delaney Clause renders it easily possible that, even when starting with identical data in risk assessments, predictions may vary over several orders of magnitude, depending on assumptions that go into each model.<sup>45</sup>

As noted, predictions made when performing quantitative risk assessment of a potential carcinogen tend to be greatly overestimated due to fear of the opposite inaccuracy: no regulator wants to underestimate the potential risk of a product, deeming it to be safer than it actually is. However, even though these carcinogenicity predictions universally tend to be inaccurate by being overestimated, they may also be quite imprecise by varying greatly from each other.

## 2. Cost-benefit analysis

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<sup>44</sup> Leticia M. Diaz, *Sucralose: The Sugar of the New Millennium – FDA’s Role: A Hindrance or a Help*, 34 N.E. L. REV. 363, 372 (2000).

<sup>45</sup> Al Meyerhoff, *The Delaney Clause: Point/Counterpoint*, 19 EPA J. 42, 42 (1993).

Many people have stated that the Delaney Clause should include a form of cost-benefit analysis.<sup>46</sup> According to these people, informed consumers should have the right to decide whether to consume a particular substance even if it is known to cause a small increase in likelihood of developing cancer.<sup>47</sup> This right particularly valid, goes the argument, because of the current technological possibility of detecting such a small likelihood of carcinogenicity and the near certainty that technology will only continue to develop, allowing for detection of even smaller likelihoods in the future.<sup>48</sup>

Supporters of allowing a cost-benefit analysis utilization in Delaney Clause regulation have argued that the current system does, and will continue to, paternalistically prevent an individual consumer from purchasing products whose benefit to her, given her personal physical and medical history (considering, *inter alia*, factors such as obesity or diabetes in a consumer's choice to purchase and consume potentially harmful artificial sweeteners), may far outweigh a small risk of developing cancer many years later. The obese or diabetic consumer may find the long-term small risk of developing cancer by consuming a product that contains saccharin to be preferable to the short-term, far more certain, risk of dangerous weight gain or blood sugar problems that would result from consuming a similar product made with sucrose.

The argument in favor of using cost-benefit analysis in Delaney Clause regulation, however, assumes perfect knowledge by consumers, an assumption that nearly never holds true. Opponents of a cost-benefit analysis mechanism in Delaney Clause regulation may argue that, in reality, most consumers are unaware of even the

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<sup>46</sup> *Sucralose: The Sugar of the New Millennium*, *supra* note 44, at 372–73.

<sup>47</sup> *Id.*

<sup>48</sup> *Id.* (using the example that a diabetic may continue to consume products containing saccharin, aware of the substance's potential carcinogenicity, rather than consuming products containing sugar, which nearly certainly would cause harm, or avoid eating any sweetened foods).

most basic risks associated with various products. Consumers often tend to believe that, if a product is on the market, it is safe for human consumption. If FDA suddenly were to begin permitting potential carcinogenic substances to be marketed and consumed, opponents could argue, the public still may assume all marketed substances to be harmless.

Even if a consumer were aware of the simple fact that a substance may be somewhat carcinogenic, the chance that he will both know and understand the exact risk to the public at large is quite small, and the likelihood that he will know and understand the risk to himself in particular (considering his age, gender, race, family history, health, eating and exercise habits, etc.) is nearly nonexistent.

Such an information problem is not unsolvable, however. The benefits of permitting cost-benefit analysis for substances that only have a small, even borderline-trivial, possibility of carcinogenicity are great. If FDA were to undertake a public information campaign regarding their new strategy, and perhaps develop a website on which information could be obtained for risk to an individual of consuming a product given her individual factors and the amount of the product she consumes, the public certainly would have much more access to knowledge of a product's particular risk to herself.

Labels on products containing the potential carcinogenic substance would be necessary as well to inform potential consumers of the risk of carcinogenicity, possibly with some form of coding to allow consumers to determine which potential carcinogens pose the greatest risks, and which merely pose risks that only barely failed being small enough to be ruled *de minimis*.



This would involve much work on FDA's part. The agency would need to determine not only the fact that a particular substance is potentially carcinogenic, but the exact potential harm to various subgroups of the population. FDA would be required to complete an information campaign and mandate labels on potentially carcinogenic products. Whether such a strategy, however beneficial it may be, will ever come to pass seems unlikely, due to both the controversy it almost certainly would cause and the extra work and expenditures it would require on FDA's part.

## II. Cancer

Cancer is one of the most feared diagnoses of patients worldwide. Many people are rightfully concerned about the potential of various foods to cause cancer. Before examining such potential, it is important to learn some background information about cancer.

### A. United States statistics

The estimated number of new cases of cancer diagnosed in the United States in 2010 was 1,529,560.<sup>49</sup> Roughly 11.4 million Americans who have had cancer of some form were alive in January 2006.<sup>50</sup> Approximately 569,490 people were expected to die of cancer in the United States in 2010, giving an approximate daily death rate of roughly 1,500 people per day.<sup>51</sup>

Cancer, aside from costing people their lives, is quite costly monetarily due to both treatment and lost productivity of cancer victims. The National Institute of Health

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<sup>49</sup> *Cancer Facts and Figures 2010*, AMERICAN CANCER SOCIETY, <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-026238.pdf> at 1 (last visited March 2011) (hereinafter "Cancer Facts and Figures").

<sup>50</sup> *Id.*

<sup>51</sup> *Id.* at 2.

estimated the overall costs of cancer to reach \$263.8 billion in 2010 alone.<sup>52</sup> Of this, \$102.8 billion would be from direct medical costs, \$20.9 billion would be from indirect morbidity costs (workers' lost productivity due to illness), and \$140.1 billion was estimated to result from indirect mortality costs (workers' lost productivity due to their premature death).<sup>53</sup>

Males have a 44.29 percent chance of developing, and being diagnosed with, cancer of an invasive site in their lifetimes; females' chance is slightly lower at 37.76 percent.<sup>54</sup> A male's risk of dying from such a cancer is 23.3 percent, while a female's chance of so dying is 19.58 percent.<sup>55</sup> The most common forms of cancer in males are prostate (16.22 percent chance of diagnosis, 2.79 percent chance of resulting death), lung and bronchus (7.67 percent chance of diagnosis, 6.95 percent chance of resulting death), colorectal (5.3 percent chance of diagnosis, 2.17 percent chance of resulting death), and bladder (3.8 percent chance of diagnosis, 0.85 percent chance of resulting death).<sup>56</sup> In females, the most common forms of cancer are breast (12.15 percent chance of diagnosis, 2.81 percent chance of resulting death), lung and bronchus (6.35 percent chance of diagnosis, 5.05 percent chance of resulting death), colorectal (4.97 percent chance of diagnosis, 2.01 percent chance of resulting death), and uterine corpus (2.58 percent chance of diagnosis, 0.53 percent chance of resulting death).<sup>57</sup>

#### B. Environmental factors

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<sup>52</sup> *Id.* at 3.

<sup>53</sup> *Id.*

<sup>54</sup> AMERICAN CANCER SOCIETY, <http://www.cancer.org/Cancer/CancerBasics/lifetime-probability-of-developing-or-dying-from-cancer> (last visited March 2011).

<sup>55</sup> *Id.*

<sup>56</sup> *Id.*

<sup>57</sup> *Id.*

Some forms of cancer are hereditary; such cancers, however, account for only five to ten percent of all cancer cases.<sup>58</sup> The focus of this paper primarily will be on cancers caused by environmental factors. Many factors influence a person's chances of developing or dying from cancer, including his socioeconomic status, race or ethnicity, and geographic location.<sup>59</sup> Regardless of race or ethnicity factors, those with lower socioeconomic status have disproportionately higher death rates from cancer than those with higher socioeconomic status; those having twelve or fewer years of formal education experience more than double the rate of cancer mortality of those with higher levels of education.<sup>60</sup>

Race also may be significant in an individual's risk of developing cancer in his lifetime. Cancer incidence rates per 100,000 members of the relevant population were, from 2002 through 2006, 550.1 for white males, 420.0 for white females, 626.0 for African-American males, 389.5 for African-American females, 334.5 for Asian-American or Pacific Islander males, 276.3 for Asian-American or Pacific Islander females, 318.4 for Native American or Alaskan males, 261.4 for Native American or Alaskan females, 430.3 for Hispanic or Latino males, and 326.8 for Hispanic or Latino females.<sup>61</sup> Cancer death rates in the same time frame per 100,000 were 226.7 for white males, 157.3 for white females, 304.2 for African-American males, 183.7 for African-American females, 135.4 for Asian-American or Pacific Islander males, 95.1 for Asian-American or Pacific Islander females, 183.3 for Native American or Alaskan males,

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<sup>58</sup> AMERICAN CANCER SOCIETY, <http://www.cancer.org/Cancer/CancerCauses/GeneticsandCancer/heredity-and-cancer> (last visited March 2011).

<sup>59</sup> Cancer Facts and Figures, *supra* note 49, at 38–40.

<sup>60</sup> *Id.* at 38.

<sup>61</sup> *Id.* at 39.

140.1 for Native American or Alaskan females, 154.8 for Hispanic or Latino males, and 103.9 for Hispanic or Latino females.<sup>62</sup>

Geographic locations also may affect a person's chances of developing, and of dying from, at least some forms of cancer. Lung cancer death rates in Kentucky (the state with the highest rates) per 100,000 are 108 in men and 56 in women, three times as high as those in Utah (with the lowest rates), which are 33 in men and 18 in women.<sup>63</sup> Disparities present in each group, however, likely are at least partially due to inequities in work, income, wealth, education, housing, standard of living, and access to proper cancer treatment and detection services.<sup>64</sup>

One in three cancer deaths are related to the victim's diet and activity.<sup>65</sup> The main risk factors for cancer are smoking, not maintaining a healthy body weight, lack of exercise, and poor food choices.<sup>66</sup> Smoking accounts for at least thirty percent of all cancer-related deaths, 87 percent of which are from lung cancer.<sup>67</sup> As compared to lifelong nonsmokers, male smokers have 23 times the risk of developing lung cancer, and female smokers have thirteen times the risk.<sup>68</sup> Lung cancer is not the only form of cancer associated with smoking, however. Smoking may increase a person's risk for at least fifteen types of cancer, including stomach, kidney, bladder, and pancreatic cancers, as well as acute myeloid leukemia.<sup>69</sup> Recent studies also have shown a possible, though still

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<sup>62</sup> *Id.*

<sup>63</sup> *Id.* at 40.

<sup>64</sup> *Id.* at 38.

<sup>65</sup> AMERICAN CANCER SOCIETY,

<http://www.cancer.org/Cancer/CancerCauses/DietandPhysicalActivity/diet-and-physical-activity> (last visited March 2011) (hereinafter "Diet and Physical Activity").

<sup>66</sup> *Id.*

<sup>67</sup> Cancer Facts and Figures, *supra* note 49, at 42.

<sup>68</sup> *Id.*

<sup>69</sup> *Id.*

uncertain, connection between smoking and colorectal, ovarian, and female breast cancers.<sup>70</sup>

Poor nutrition and lack of physical activity account for roughly one in three cancer deaths in the United States; a significant part of this causation is due to the weight increase resulting from such choices.<sup>71</sup> Certainly, as many people are aware, eating more fruits, vegetables, and whole grains while consuming less processed and red meats can reduce one's chances of developing cancer.<sup>72</sup> However, what about particular foods that may be carcinogenic or contain carcinogenic ingredients? How dangerous are these in a person's life, and how much cancer do such foods account for?

Exposure to carcinogenic agents in occupational settings accounts for roughly four percent of cancer deaths; such exposure from environmental pollutants, both manmade and naturally occurring, accounts for approximately two percent of cancer deaths.<sup>73</sup> Though the percentages sound small, they may account for up to 34,000 deaths in the United States.<sup>74</sup> The next section will examine in more detail some of the carcinogens that cause these cancer deaths, focusing on carcinogenic foods and food additives.

### III. Carcinogens

Carcinogen is a broad term, encompassing materials the exposure to which may increase the incidence of cancer.<sup>75</sup> The term may apply to such various substances as chemicals (i.e., benzene), fibrous materials (i.e., asbestos), metals and physical agents

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<sup>70</sup> *Id.*

<sup>71</sup> *Id.* at 48.

<sup>72</sup> Diet and Physical Activity, *supra* note 65.

<sup>73</sup> Cancer Facts and Figures, *supra* note 49, at 50.

<sup>74</sup> *Id.*

<sup>75</sup> *Id.*

(i.e., x-rays, ultraviolet light), or exposures linked to particular industries or occupations (i.e., nickel refining).<sup>76</sup>

Carcinogens are identified normally either by animal testing or epidemiological studies.<sup>77</sup> As discussed earlier, this paper primarily will focus on carcinogens as related to the Delaney Clause, which does not itself provide a definition for the term. The Clause fails to provide specific guidelines for how carcinogenic an additive must be to be considered a carcinogen for its purposes, largely because Congress, when enacting the Delaney Clause, could not (or at least did not) foresee the current ability of scientific technology to detect remarkably small chances of carcinogenicity in several commonly-consumed foods.

#### A. Ethyl alcohol

One commonly-consumed substance that increases the risk of cancer is ethyl alcohol (ethanol); approximately two to four percent of cancer cases are thought to be caused, either directly or indirectly, by ethyl alcohol.<sup>78</sup> A strong correlation between ethyl alcohol use and the potential for development of cancers of the esophagus, pharynx, and mouth exists, as well as a more controversial association between the use of ethyl alcohol and liver, breast, and colorectal cancers.<sup>79</sup> The United States Department of Health and Human Services has listed ethyl alcohol as a known carcinogen. Obviously, however, ethyl alcohol is not forbidden under the Delaney Clause, having been declared GRAS by FDA. This section will examine some of the carcinogenic potential of ethyl alcohol.

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<sup>76</sup> *Id.* at 50–51.

<sup>77</sup> *Id.* at 51.

<sup>78</sup> *Alcohol Alert*, NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM, <http://pubs.niaaa.nih.gov/publications/aa21.htm> (last visited March 2011).

<sup>79</sup> *Id.*

### 1. Upper digestive tract cancers

Epidemiological research has shown a strong correlation between the use of ethyl alcohol and occurrences of cancer in the upper digestive tract (esophagus, mouth, pharynx, and larynx).<sup>80</sup> Roughly 75 percent of esophageal cancer cases in the United States are due to consumption of ethyl alcohol, normally chronic alcohol abuse.<sup>81</sup> Similar abuse of ethyl alcohol is thought to be responsible for nearly one-half of all cases of cancer of the mouth, larynx, and pharynx.<sup>82</sup> The United States National Cancer Institute has stated that the risk of developing these cancers, as well as the risk of liver cancer, increases after only approximately one daily drink (twelve ounces of regular beer, five ounces of wine, or 1.5 ounces of eighty-proof liquor) for women and after two such daily drinks for men.<sup>83</sup>

### 2. Liver cancer

Heavy use of ethyl alcohol also has been associated with liver cancer, though the cancer normally is caused by cirrhosis, which in turn is caused by alcohol abuse.<sup>84</sup> Roughly five percent of those with cirrhosis develop liver cancer as a result.<sup>85</sup> Some believe that up to 36 percent of cases of liver cancer in the United States are caused by ethyl alcohol abuse.<sup>86</sup>

### 3. Breast cancer

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<sup>80</sup> *Id.*

<sup>81</sup> *Id.*

<sup>82</sup> *Id.*

<sup>83</sup> *Cancer Trends Progress Report – Alcohol Consumption*, NATIONAL CANCER INSTITUTE, [http://progressreport.cancer.gov/doc\\_detail.asp?pid=1&did=2007&chid=71&coid=706&mid=](http://progressreport.cancer.gov/doc_detail.asp?pid=1&did=2007&chid=71&coid=706&mid=).

<sup>84</sup> *Alcohol Alert*, *supra* note 78.

<sup>85</sup> *Liver Cancer*, THE UNIVERSITY OF TENNESSEE MEDICAL CENTER, <http://www.utmedicalcenter.org/cms/Liver+Cancer==/571.html> (last visited March 2011).

<sup>86</sup> *Id.*

Chronic use of ethyl alcohol may increase a woman's chance of developing breast cancer by roughly ten percent.<sup>87</sup> Some studies, however, have found that ethyl alcohol has no effect on likelihood of developing breast cancer.<sup>88</sup> Recent studies have shown that ethyl alcohol increases levels of estrogen in premenopausal women, which may lead to an increased risk of developing breast cancer.<sup>89</sup> Institutions listing ethyl alcohol as a risk factor for developing breast cancer include the American Cancer Society,<sup>90</sup> Cancer Research UK,<sup>91</sup> the National Cancer Institute,<sup>92</sup> and the American Society of Clinical Oncology.<sup>93</sup> If a woman consumes an average of two drinks per day, her risk for developing breast cancer is approximately eight percent higher than if she averages one drink per day.<sup>94</sup>

#### 4. Colon cancer

A small correlation between consumption of ethyl alcohol and a risk of developing colon cancer appears to exist; however, although the epidemiological studies showing the existence of a correlation controlled for fiber and other dietary factors, the studies are insufficient to show causality.<sup>95</sup> Despite the lack of complete certainty, many noteworthy institutions list ethyl alcohol as a risk factor for colorectal cancer, including

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<sup>87</sup> *Id.*

<sup>88</sup> *Id.*

<sup>89</sup> *Id.*

<sup>90</sup> *What are the risk factors for breast cancer?*, AMERICAN CANCER SOCIETY, <http://www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-risk-factors> (last visited March 2011).

<sup>91</sup> *Definite breast cancer risks*, CANCER RESEARCH UK, <http://www.cancerhelp.org.uk/type/breast-cancer/about/risks/definite-breast-cancer-risks> (last visited March 2011).

<sup>92</sup> *What You Need To Know About Breast Cancer*, NATIONAL CANCER INSTITUTE, <http://www.cancer.gov/cancertopics/wyntk/breast/page4> (last visited March 2011).

<sup>93</sup> *Guide to Breast Cancer*, AMERICAN SOCIETY OF CLINICAL ONCOLOGY, [http://www.cancer.net/patient/Cancer%20Types/Cancer.Net%20Guide%20to%20Cancer%20PDFs/Cancer.Net\\_Guide\\_to\\_Breast\\_Cancer\\_PDF.pdf](http://www.cancer.net/patient/Cancer%20Types/Cancer.Net%20Guide%20to%20Cancer%20PDFs/Cancer.Net_Guide_to_Breast_Cancer_PDF.pdf), at 6 (last visited March 2011).

<sup>94</sup> *Consumption of Alcoholic Beverages and Risk of Breast Cancer in Women*, COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT, <http://www.advisorybodies.doh.gov.uk/pdfs/alco04nontech.pdf>, at 1 (last visited March 2011).

<sup>95</sup> *Alcohol Alert*, *supra* note 78.



the National Cancer Institute,<sup>96</sup> the Colorectal Cancer Coalition,<sup>97</sup> Cancer Research,<sup>98</sup> the Memorial Sloan-Kettering Cancer Center,<sup>99</sup> the American Cancer Society,<sup>100</sup> and the Mayo Clinic.<sup>101</sup>

## 5. Other cancers

Some studies have shown a correlation between chronic abuse of ethyl alcohol and an increased risk in developing cancer of the stomach, pancreas, and lungs; the association is weak, however, and most studies have shown no such correlation.<sup>102</sup> According to some studies, a higher intake of ethyl alcohol also has been associated with cancer of the endometrium,<sup>103</sup> ovaries,<sup>104</sup> prostate,<sup>105</sup> and small intestines.<sup>106</sup> Such associations are far from certain, and studies frequently have produced contrary results, showing ethyl alcohol either not to be a factor or even to have an inverse association with the form of cancer, providing an antioxidant effect.<sup>107</sup>

## B. Artificial sweeteners

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<sup>96</sup> *Cancer Risk: Understanding the Puzzle*, NATIONAL CANCER INSTITUTE, [http://understandingrisk.cancer.gov/a\\_Colon/01.cfm](http://understandingrisk.cancer.gov/a_Colon/01.cfm) (last visited March 2011).

<sup>97</sup> *Assessing Your Risk for Colorectal Cancer*, COLORECTAL CANCER COALITION, <http://fightcolorectalcancer.org/awareness/patients/prevention/risk> (last visited March 2011).

<sup>98</sup> *Food Types and Bowel Cancer*, Cancer Research UK, <http://www.cancerhelp.org.uk/type/bowel-cancer/about/risks/food-types-and-bowel-cancer> (last visited March 2011).

<sup>99</sup> *Colorectal Cancer: Risk Reduction*, MEMORIAL SLOAN-KETTERING CANCER CENTER, <http://www.mskcc.org/mskcc/html/310.cfm> (last visited March 2011).

<sup>100</sup> *What Are the Risk Factors for Colorectal Cancer?*, AMERICAN CANCER SOCIETY, [http://web.archive.org/web/20080419135519/http://www.cancer.org/docroot/CRI/content/CRI\\_2\\_4\\_2X\\_What\\_are\\_the\\_risk\\_factors\\_for\\_colon\\_and\\_rectum\\_cancer.asp](http://web.archive.org/web/20080419135519/http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_What_are_the_risk_factors_for_colon_and_rectum_cancer.asp) (last visited March 2011).

<sup>101</sup> *Colon cancer: Risk factors*, MAYO CLINIC, <http://www.mayoclinic.com/health/colon-cancer/DS00035/DSECTION=risk-factors> (last visited March 2011).

<sup>102</sup> *Alcohol Alert*, *supra* note 78.

<sup>103</sup> *Review of Alcohol: Association with Endometrial Cancer*, UK DEPARTMENT OF HEALTH, <http://www.advisorybodies.doh.gov.uk/pdfs/alcend.pdf>, at 2–3 (last visited March 2011).

<sup>104</sup> *Alcohol consumption and cancer risk*, BANDOLIER, <http://www.medicine.ox.ac.uk/bandolier/booth/hliving/alccan.html> (last visited March 2011).

<sup>105</sup> *Study links alcohol, prostate cancer*, ABC NEWS, <http://www.abc.net.au/news/stories/2009/03/14/2516235.htm> (last visited March 2011).

<sup>106</sup> Clark C. Chen, Alfred I. Neugut, and Heidrun Rotterdam, *Risk Factors for Adenocarcinomas and Malignant Carcinoids of the Small Intestine: Preliminary Findings*, 3 CANCER EPIDEMIOLOGY, BIOMARKERS, & PREVENTION 205, 206 (1994).

<sup>107</sup> *See, e.g., Review of Alcohol, supra* note 103, at 3–8.

Some of the most controversial food additives, though they are some of the most clinically tested, are artificial sweeteners, or sugar substitutes. The six sugar substitutes approved for use in the United States by FDA are saccharin, aspartame, sucralose, neotame, and acesulfame potassium (all of which are artificial sweeteners)<sup>108</sup> and stevia (which is a natural sugar substitute). Not all sugar substitutes are carcinogenic; in fact, though they are often some of the substances most associated with carcinogenicity, most have been shown not to be carcinogenic whatsoever.

All sugar substitutes, however, like most food additives of any sort, have been heavily studied, tested, and regulated by FDA at some point. FDA regulates sugar substitutes as food additives. Stevia is a natural substance in use before 1958 and, hence, is exempt from Delaney Clause regulation because it falls under FDA's GRAS policy. The other sweeteners, however, do fall under the Delaney Clause and, if the Clause is applied strictly, the sugar substitutes must not be carcinogenic whatsoever to remain on the market and be permissible for public consumption.

Several natural sugar substitutes exist; some of the most common of these in the United States include maltitol, xylitol, isomalt, sorbitol, and inulin. FDA long ago banned some of the more uncontroversially-considered dangerous (due either to potential toxicity or carcinogenicity) artificial sweeteners, including dulcin and P-4000. Other such sugar substitutes, such as lead acetate, were considered dangerous long ago and are no longer in use. The primary focus here will be on the regulation of FDA-approved sugar substitutes (including, for the sake of comparison, even those sweeteners for which

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<sup>108</sup> Jason Iuliano, *Killing Us Sweetly: How to Take Industry out of the FDA*, 6 J. FOOD L. & POL'Y 31, 46 (2010).

no evidence exists as to potential carcinogenicity) and on cyclamate, which FDA banned in 1969.

#### 1. Sucralose

Sucralose, most commonly known by its brand name, Splenda, is a non-nutritive, high-intensity (roughly six hundred times sweeter than sucrose, or table sugar) sweetener that is made from sucrose.<sup>109</sup> The body, however, does not metabolize sucralose as it does sucrose, so sucralose is able to provide the taste of sucrose without the calories.<sup>110</sup> Sucralose is not metabolized, but instead moves rapidly through the body; it does not accumulate in the body.<sup>111</sup> Sucralose provides a further benefit for diabetic consumers: the sweetener appears not to raise blood sugar.<sup>112</sup> Sucralose can be used for baking purposes because of its stability to heat.<sup>113</sup> The sweetener has become quite popular in recent years.

FDA approved sucralose for use in the United States on April 1, 1998 after more than 110 human and animal studies showed it to be completely safe and free from any harmful side effects.<sup>114</sup> Twenty-eight countries already had permitted sucralose to be sold on the market before FDA's approval, including Canada, which already had been permitting its use for seven years.<sup>115</sup> For a new food product to be approved by FDA for use in the United States, the substance's sponsor (for sucralose, McNeil served as the sponsor) must present data that the substance is safe for its intended use; FDA then considers factors such as likely human exposure to the substance, toxicological results,

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<sup>109</sup> *Sucralose: The Sugar of the New Millennium*, *supra* note 44, at 373–74.

<sup>110</sup> *Sugar Substitutes: Sucralose*, CALORIE CONTROL COUNCIL, <http://www.caloriecontrol.org/sweeteners-and-lite/sugar-substitutes/sucralose> (last visited Apr. 14, 2011).

<sup>111</sup> *Id.*

<sup>112</sup> *Id.*

<sup>113</sup> *Id.*

<sup>114</sup> 63 Fed. Reg. 16417 (1998).

<sup>115</sup> *Sucralose: The Sugar of the New Millennium*, *supra* note 44, at 377.

and other submitted data.<sup>116</sup> Because of the extensive research and data available for sucralose, many believe that FDA should have approved the sweetener rather quickly, and at times have criticized FDA's delay in approving the substance as sheer sluggishness.<sup>117</sup>

## 2. Stevia

Stevia is the newest addition to the United States market of sugar substitutes. It is a natural herb that is roughly two hundred to three hundred times sweeter than sugar.<sup>118</sup> FDA forbade the usage of stevia as an additive in Celestial Seasonings teas in 1986 and then banned the substance as an unsafe food additive in 1991.<sup>119</sup> Some have asserted, however, that the stevia ban actually had political motives: to promote the usage of aspartame without it being forced to compete with stevia.<sup>120</sup> After pro-stevia activists fought to reintroduce the sugar substitute, FDA allowed stevia to be sold and consumed as a dietary supplement beginning in September 1995.<sup>121</sup> For a great deal of time, however, stevia could be purchased only as a dietary supplement; FDA did not permit the public to purchase products containing stevia as a sweetener.<sup>122</sup> As was true regarding sucralose, many other countries used stevia safely for years before its usage was approved in the United States.<sup>123</sup>

Although no evidence of stevia's carcinogenicity has been discovered, FDA asserted its basis of reluctance to approve the substance as a sweetener to be in part on a

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<sup>116</sup> 63 Fed. Reg. 16417, 16418.

<sup>117</sup> *Sucralose: The Sugar of the New Millennium*, *supra* note 44, at 378.

<sup>118</sup> *Import Alert 45-06*, UNITED STATES FOOD AND DRUG ASSOCIATION, [http://www.accessdata.fda.gov/cms\\_ia/importalert\\_119.html](http://www.accessdata.fda.gov/cms_ia/importalert_119.html) (last visited April 2011).

<sup>119</sup> *Sucralose: The Sugar of the New Millennium*, *supra* note 44, at 384.

<sup>120</sup> *Id.* at 384 n.120.

<sup>121</sup> *Id.* at 385.

<sup>122</sup> *Id.* at 386.

<sup>123</sup> *Id.* at 385–86.

Brazilian study that found mice that were fed with stevia to have potentially reduced fertility.<sup>124</sup> Therefore, FDA declared that the “[a]vailable toxicological information on stevia is inadequate to demonstrate its safety as a food additive or to affirm its status as GRAS.”<sup>125</sup>

However, although stevia was not determined to be safe for usage as a food additive, its required regulation was less strict under the Dietary Supplement Health and Education Act of 1994 (DSHEA) and, hence, FDA declared that “with regard to its use in dietary supplements, dietary ingredients, including stevia, are not subject to food additive regulations.”<sup>126</sup> Therefore, counterintuitively, customers were permitted to purchase children’s vitamins that contained stevia as an ingredient, but not if the vitamins were declared to be sweetened with stevia (or even if advertisements for the vitamins simply flaunted their sweetness, particularly in comparison to other vitamins).<sup>127</sup> In December 2008, FDA finally declared the substance to be GRAS, allowing stevia to be sold and consumed as a food additive.<sup>128</sup> Currently, the sweetener is marketed most prominently as Truvia, but also is sold under the names SweetLeaf, Only Sweet, PureVia, Rebiana, and Reb-A.

### 3. Aspartame

One of the most controversial, and perhaps even infamous, artificial sweeteners is aspartame. Most commonly known under the brand names of Equal or NutraSweet, aspartame also is a prominent ingredient in many frequently-consumed foods and

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<sup>124</sup> Cassandra Burke Robertson, *Separating Snake Oil from Therapeutic Supplements – The Nexus between Litigation and Regulation in the Dietary Supplement Industry*, 35 U. TOL. L. REV. 317, 327 (2003).

<sup>125</sup> *FDA Import Alert 45-06*, *supra* note 118.

<sup>126</sup> *Id.*

<sup>127</sup> *Separating Snake Oil from Therapeutic Supplements*, *supra* note 124, at 327.

<sup>128</sup> *GRAS Notice Inventory No. 287*, FOOD AND DRUG ADMINISTRATION, <http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=grasListing&id=287> (last visited April 2011).

beverages, including diet colas, gum and mints, yogurt, juices, cereals, and gelatin desserts.

a. Approval history

G.D. Searle and Company discovered the substance now known as aspartame in 1965 while researching amino acids.<sup>129</sup> FDA approved aspartame as a food sweetener in 1974.<sup>130</sup> After several scientists questioned the sweetener's safety, however, FDA stayed its approval in 1975 and prepared for an evidentiary hearing.<sup>131</sup> When FDA audited Searle's clinical methods, the agency found what it described as sloppy research methods on aspartame: the research contained numerous discrepancies, including mixed favorability toward aspartame, numbers that did not add up correctly, and questionable testing plans.<sup>132</sup>

A hearing before a public board of inquiry considered three questions: (1) whether aspartame (by itself or paired with glutamate, with which it commonly had been combined) could cause mental retardation, brain damage, or damage to neuroendocrine regulatory systems; (2) whether aspartame may cause brain neoplasms in laboratory rats; and (3) whether, upon considering the answers to the first two questions, aspartame should be allowed to be used in foods and, if so, what conditions of use and labeling requirements should be enforced.<sup>133</sup>

The board found, by Searle's research, that aspartame did not cause brain or endocrine damage, but it was concerned about the substance's potential

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<sup>129</sup> David Ellender, *A Class-Action Lawsuit against Aspartame Manufacturers: A Realistic Possibility or Just a Sweet Dream for Tort Lawyers*, 18 REGENT U.L. REV. 175, 192 (2005).

<sup>130</sup> 21 C.F.R. § 172.804 (1975).

<sup>131</sup> *A Class-Action Lawsuit against Aspartame Manufacturers*, *supra* note 129, at 192.

<sup>132</sup> *Id.* at 192–93.

<sup>133</sup> 46 Fed. Reg. 38285, 38286 (1981).

carcinogenicity.<sup>134</sup> The board believed that the three studies that Searle conducted (the only evidence they were able to consider) showed an unusually high occurrence of brain tumors and that a dose-effect relationship may exist between aspartame and the tumors.<sup>135</sup> Thus, the board concluded that further testing should be performed before aspartame could be safely marketed.<sup>136</sup>

However, after extensive pressure from Searle, including the threat of a lawsuit against FDA, the commissioner overruled the board of inquiry and, on July 18, 1981, approved aspartame for use in sweetening foods.<sup>137</sup> In 1982, Searle requested approval for aspartame to be used in sweetening carbonated drinks,<sup>138</sup> which FDA quickly approved, even denying requests for a hearing from the numerous objectors to the approval.<sup>139</sup>

b. Safety

Aspartame is composed of phenylalanine and aspartic acid.<sup>140</sup> According to the NutraSweet company, aspartame is not harmful in any way; the company even has referenced several organizations confirming its safety (including FDA, Health Canada, the European Commission's Scientific Committee on Food, World Health Organization Joint Expert Committee on Food Additives, and the United Nations' Food and Agricultural Organization).<sup>141</sup> Much of the company's reliance is on antiquated sources,

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<sup>134</sup> 1980 New Matters, FOOD DRUG COSM. L. REP., Aspartame (Board's Initial Decision), ¶ 38072, 38346, 38349.

<sup>135</sup> *Id.* at 38346–48.

<sup>136</sup> *Id.* at 38349.

<sup>137</sup> 46 Fed. Reg. 38301–03.

<sup>138</sup> 47 Fed. Reg. 46140 (1982).

<sup>139</sup> 21 C.F.R. § 172.804(c)(6) (1984).

<sup>140</sup> *What is aspartame made of?*, THE NUTRASWEET COMPANY, <http://www.nutrasweet.com/articles/article.asp?Id=36> (last visited March 2011).

<sup>141</sup> *Is aspartame safe?*, THE NUTRASWEET COMPANY, <http://www.nutrasweet.com/articles/article.asp?Id=45> (last visited March 2011).

however, including the FDA statement, which places great emphasis simply on the 1981 approval.<sup>142</sup> It is difficult, therefore, for many to accept NutraSweet's assertion of aspartame's safety as uncontroverted.

FDA's maximum acceptable daily limit of aspartame has been set at fifty milligrams per kilogram of body weight, the equivalent of sixteen twelve-ounce cans of soda for a 150-pound individual.<sup>143</sup> According to NutraSweet, when aspartame enters the body, it "breaks down into its components – the amino acids, aspartic acid and phenylalanine, and methanol – which are then absorbed into the blood. These components are used in the body in exactly the same ways as when they are also obtained from common foods and beverages. Neither aspartame nor its components accumulate in the body over time."<sup>144</sup>

Although many claims of aspartame's dangers are from outlandish sources (some of which evoke conspiracy-theory-type arguments), some are more reliable. The American Academy of Pediatrics has expressed fear of the risk of birth defects from women with undiagnosed phenylketonuria (a genetic disorder causing phenylalanine to build up in the bloodstream and brain tissue, leading to mental retardation and various nervous system problems).<sup>145</sup> Other sources, such as Mercola, have expressed concern about aspartame's effects on all individuals (with or without phenylketonuria), believing the substance not to be safely processed by the body after digestion because certain amino acids that normally are present with phenylalanine in foods, and helping to break it down, are not present with it in aspartame, causing phenylalanine to build up in the brain

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<sup>142</sup> *A Class-Action Lawsuit against Aspartame Manufacturers*, *supra* note 129, at 195.

<sup>143</sup> *Id.* at 196.

<sup>144</sup> *How is aspartame handled by the body?*, THE NUTRASWEET COMPANY, <http://www.nutrasweet.com/articles/article.asp?Id=37> (last visited March 2011).

<sup>145</sup> *A Class-Action Lawsuit against Aspartame Manufacturers*, *supra* note 129, at 196–97.



and bloodstream.<sup>146</sup> Others have expressed fear about the effects on a child in the womb when its mother consumes aspartame-containing products; because of the child's low weight, it might easily exceed the maximum recommended amount of aspartame even at a relatively low level of aspartame consumption by the mother.<sup>147</sup>

Aspartame remains permissible for consumption in the United States. Though no conclusive evidence exists of its carcinogenicity or of other harmful effects, many consumers are wary of the sweetener.

#### 4. Cyclamate

Cyclamate is an artificial sweetener that is less sweet than, but (at least according to some) lacks the bitter aftertaste of, its more well-known counterpart, saccharin.<sup>148</sup> FDA first approved cyclamate for public consumption in 1950 for use by those with diabetes or severe obesity; in 1958, in spite of the relatively short history of the safe use of the substance, FDA reclassified cyclamate as an acceptable food additive.<sup>149</sup> Women's desire for a more slender figure, beginning in the 1960s, led to a situation in which cyclamate was being consumed, at one point, by 75% of the United States population.<sup>150</sup> The sweetener was no longer for a small subgroup of the population, but instead was being used by a majority of people in the United States.

The wariness of Americans regarding unsafe food additives at the time, however, led to cyclamate becoming a suspect product in the 1960s.<sup>151</sup> FDA requested that the National Academy of Sciences perform periodic reviews of the substance; in these

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<sup>146</sup> See, e.g., *Aspartame Disease: An FDA-Approved Epidemic*, MERCOLA, <http://articles.mercola.com/sites/articles/archive/2004/01/07/aspartame-disease.aspx> (last visited April 2011).

<sup>147</sup> See DR. H.J. ROBERTS, *ASPARTAME DISEASE: AN IGNORED EPIDEMIC* (2001).

<sup>148</sup> Allan Mazur and Kevin Jacobson, *Looking Back: Cyclamate*, 10 RISK 95, 95 (1999).

<sup>149</sup> *Id.*

<sup>150</sup> *Id.*

<sup>151</sup> See, e.g., JAMES S. TURNER, *THE CHEMICAL FEAST* (1970).

reviews, the Academy confirmed cyclamate's general safety, but warned that public distribution may lead to unpleasant side effects (such as diarrhea) and potentially harmful unknown long-term effects.<sup>152</sup>

A 1968 study showing chromosome breakage in rats after exposure to a metabolite of cyclamate caused FDA to provide a recommended daily upper limit of cyclamate of 50 milligrams per kilogram of body weight.<sup>153</sup> Another study showed egg deformities when cyclamate was injected into chicken eggs; FDA Commissioner Herbert Ley took no action to regulate the sweetener more strictly, and Abbott Laboratories spokesmen declared cyclamate still to be safe.<sup>154</sup> However, shortly after the release of the study on chicken eggs, Abbott Laboratories released the results of a study showing a mixture with a ratio of ten parts cyclamate to one part saccharin to result in bladder tumors, some of which were cancerous.<sup>155</sup>

Thus, on October 18, 1969, Secretary of Health, Education and Welfare Robert Finch announced at a press conference that usage of cyclamate did, in fact, indicate carcinogenicity and, therefore, approval of the substance would be a violation of the Delaney Clause.<sup>156</sup> FDA would not permit cyclamate to be used in nonprescription food or drinks; products containing cyclamate would be recalled.<sup>157</sup> The following year, FDA also forbade usage of the sweetener in prescription products.<sup>158</sup>

We now know that injection of a substance into a chicken egg does not provide reliable data for potential human birth defects and that cyclamate does not actually cause

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<sup>152</sup> *Looking Back: Cyclamate*, *supra* note 148, at 96.

<sup>153</sup> *Id.*

<sup>154</sup> *Id.* at 96–97.

<sup>155</sup> *Id.* at 97.

<sup>156</sup> *Id.*

<sup>157</sup> *Id.*

<sup>158</sup> *Id.*

birth defects in mammals.<sup>159</sup> Many additional studies were conducted for further examination of cyclamate's potential carcinogenicity, but none showed a link to bladder tumors; those that were present in the originally-studied rats allegedly may have been caused by cage contamination, parasites or stones in the rats' bladders, or another outside factor.<sup>160</sup>

Thus, in 1984, FDA's Cancer Assessment Committee declared cyclamate not to be carcinogenic.<sup>161</sup> FDA asked the National Academy of Sciences to evaluate the substance's potential to cause cancer; the Academy determined that cyclamate is not a carcinogen but that it may be a co-carcinogen (meaning that it may promote the action of any carcinogens that already exist in the body).<sup>162</sup> Whether the sweetener caused genetic damage remained uncertain.<sup>163</sup> Although, by 1989, cyclamate appeared to be safe and not carcinogenic, FDA still has refused to lift the ban on the sweetener, particularly after the development of additional non-carcinogenicity-related concerns (including a possible risk of links between cyclamate and both testicular atrophy and elevated blood pressure).<sup>164</sup> The existence of additional sweeteners that are approved by FDA likely is another reason for FDA's reluctance to lift the ban on cyclamate: the agency does not consider cyclamate to be a necessary addition to the food supply for any legitimate reason.

## 5. Neotame

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<sup>159</sup> *Id.* at 97–98.

<sup>160</sup> Calorie Control Council and Abbott Laboratories, Food Additive Petition for Cyclamate, 2A3672 (1982).

<sup>161</sup> *Looking Back: Cyclamate*, *supra* note 148, at 98.

<sup>162</sup> NATIONAL ACADEMY OF SCIENCES, EVALUATION OF CYCLAMATE FOR CARCINOGENICITY (1985).

<sup>163</sup> *Looking Back: Cyclamate*, *supra* note 148, at 98–99.

<sup>164</sup> *Id.* at 99.

Neotame, made by NutraSweet, is an artificial sweetener that is approximately eight thousand times sweeter than table sugar.<sup>165</sup> It has moderate heat stability and appears not to accumulate in the body whatsoever.<sup>166</sup> Neotame does produce methanol when metabolized; however, the small amount of the substance needed to sweeten foods lead it to produce a smaller amount of methanol than do commonly-consumed natural foods such as fruit or vegetable juices.<sup>167</sup> Neotame does have the often-disliked aftertaste that is common to artificial sweeteners. The sweetener actually is a modified version of aspartame but is more stable and used in much smaller amounts; neotame contains the same elements found in aspartame with the addition of two amino acids and two organic groups.

FDA approved neotame for general use in July 2002 after over one hundred corporate-sponsored studies showed its safety for the public, including diabetics and pregnant women.<sup>168</sup> These studies included those performed both on humans and on animals using far higher dosages than expected to be consumed by the general public; laboratory animals received the equivalent of fifty thousand cans of neotame-sweetened soda every day for a lifetime.<sup>169</sup> Unlike aspartame, neotame needs no warning for individuals with phenylketonuria, as it does not produce the same harmful effects on members of this population as does aspartame.<sup>170</sup> The consumer advocacy group Center

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<sup>165</sup> *Neotame: A Scientific Overview*, THE NUTRASWEET COMPANY, [http://www.neotame.com/pdf/neotame\\_science\\_brochure\\_US.pdf](http://www.neotame.com/pdf/neotame_science_brochure_US.pdf), at 2 (last visited March 2011).

<sup>166</sup> *Id.* at 3.

<sup>167</sup> *Id.*

<sup>168</sup> *Id.* at 2.

<sup>169</sup> *Id.*

<sup>170</sup> *Id.*

for Science in the Public Interest has stated that it considers only neotame and sucralose to be safe artificial sweeteners.<sup>171</sup>

## 6. Acesulfame Potassium

Acesulfame potassium, commonly known as acesulfame-K, is an artificial sweetener that is roughly two hundred times sweeter than table sugar<sup>172</sup> (which is approximately the same intensity as aspartame). Karl Clauss, a German chemist, discovered the sweetener in 1967. Acesulfame potassium is used throughout the world, available as a dry powder to be used in foods and beverages, and is an ingredient in many frequently-consumed foods and beverages.<sup>173</sup> Studies have shown acesulfame potassium not to accumulate in the body.<sup>174</sup>

Acesulfame potassium almost never is used to sweeten foods alone, but instead normally is used in conjunction with other sweeteners. It frequently is blended with sucralose to sweeten foods and beverages.<sup>175</sup> FDA began approving acesulfame potassium for use as an additive in 1988 and finally approved it for use in soft drinks in 1998.<sup>176</sup> The sweetener currently is available for general consumption in the United States.

The National Toxicology Program performed a rodent study on acesulfame potassium that showed no increased incidence of tumors due to consumption of the

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<sup>171</sup> *Chemical Cuisine: Learn about Food Additives*, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, <http://www.cspinet.org/reports/chemcuisine.htm> (last visited March 2011).

<sup>172</sup> *Toxicity Studies of Acesulfame Potassium*, NATIONAL TOXICOLOGY PROGRAM, [http://ntp.niehs.nih.gov/files/GMM2\\_Web.pdf](http://ntp.niehs.nih.gov/files/GMM2_Web.pdf), at 11 (last visited March 2011).

<sup>173</sup> *Id.*

<sup>174</sup> *Id.*

<sup>175</sup> *Testing Needed for Acesulfame Potassium, an Artificial Sweetener*, MYRA L. KARSTADT, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1570055/> (last visited March 2011).

<sup>176</sup> *Id.*

sweetener.<sup>177</sup> The laboratory rats in the nine-month study were given a diet of three percent acesulfame potassium,<sup>178</sup> enough of the substance to be equivalent to a human consuming over 1300 cans of acesulfame potassium-sweetened soda each day. Many people believe that insufficient evidence of the sweetener's safety exists, however, and have called for further studies regarding whether acesulfame potassium is safe for public consumption.<sup>179</sup>

## 7. Saccharin

The artificial sweetener that is most often associated with carcinogenicity is saccharin. It is most commonly marketed and sold as Sweet 'N Low. Saccharin's basic substance is known as benzoic sulfilimine, which has little to no food energy and is much sweeter than sucrose. Its primary practical downfalls are its unpleasant aftertaste and instability when heated. The history and regulation of saccharin will be examined in particular detail, with especial concentration on the excessive politicization of its approval.

### a. History

In 1878, the chemist Constantin Fahlberg first produced saccharin while working on coal tar derivatives.<sup>180</sup> Because the substance is roughly 350 times sweeter than sugar, it attracted users in the early 1900s, including canners desiring to use it to sweeten fruits and vegetables.<sup>181</sup> Saccharin's usage became widespread during the sugar shortages of World War I. During the 1960s and 1970s, it became even more popular as a calorie-free

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<sup>177</sup> *Toxicity Studies*, *supra* note 172, at 4.

<sup>178</sup> *Id.*

<sup>179</sup> *See, e.g., Testing Needed for Acesulfame Potassium, an Artificial Sweetener*, *supra* note 175.

<sup>180</sup> Richard A. Merrill and Michael R. Taylor, *Saccharin: A Case Study of Government Regulation of Environmental Carcinogens*, 5 VA. J. NAT. RESOURCES L. 1, 25 (1985) (hereinafter *Saccharin: A Case Study*).

<sup>181</sup> *Id.*

alternative to sugar for dieters. Although the Office of Environmental Health Hazard Assessment placed saccharin on the list of chemicals known to cause cancer in 1989, it was delisted as such on April 6, 2001.

b. Regulation

i. Department of Agriculture

The first United States agency to regulate saccharin was not FDA; instead, it was the United States Department of Agriculture. Dr. Harvey Wiley, who at that time was the head of the Agriculture Department's Bureau of Chemistry, and is considered the father of food and drug regulation in the United States, was the first to raise questions about the sweetener's safety in 1907.<sup>182</sup> President Theodore Roosevelt, however, who did not believe in mincing words, stated, quite simply, that "[a]nybody who says that saccharin is injurious to health is an idiot."<sup>183</sup> Understandably, Dr. Wiley was reluctant to pursue his concerns about saccharin's potential safety hazards very far after President Roosevelt's statement, and certainly was not likely to declare the sweetener to be unsafe for public consumption.

The Secretary of Agriculture later referred the matter to the Referee Board of Consulting Scientific Experts, which concluded that chronic consumption of saccharin at a level of more than 0.3 grams per day could impair digestion.<sup>184</sup> In April 1911, after President Roosevelt was no longer in office, the Secretary declared saccharin to be an "added poisonous or other added deleterious ingredient" that would cause food to be adulterated.<sup>185</sup>

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<sup>182</sup> *Id.* at 25–26.

<sup>183</sup> HARVEY W. WILEY, AN AUTOBIOGRAPHY 240–41 (1930).

<sup>184</sup> DEPARTMENT OF AGRICULTURE, SACCHARIN IN FOOD, FOOD INSPECTION DECISION 135 (1911).

<sup>185</sup> *Id.*

Later, after discovering that saccharin consumption could not possibly exceed the 0.3 gram daily level, he retracted his finding that saccharin could harm health, but he still maintained that it would adulterate foods by lowering their quality as compared to foods that were made with sucrose.<sup>186</sup> The Secretary maintained, however, that physicians still would be permitted to prescribe saccharin, and products that contained it, for those who are required to avoid sugar due to diabetes or other medical reasons.<sup>187</sup>

ii. FDA

The first long-term study of saccharin's toxicity was completed in 1951.<sup>188</sup> In August 1955, the Food Protection Committee, after a review of the sweeteners performed at the request of FDA, declared both saccharin and cyclamate to be nearly completely safe; in particular, the Committee declared that the possible digestive problems that were associated with saccharin would only present themselves at extremely high dose levels (far greater than the amount of the sweetener that one normally would ingest) and that data on chronic effects did not indicate any chance of harm at levels that people actually were likely to consume.<sup>189</sup> The Food Protection Committee did, however, recommend that further study of saccharin (and of cyclamate) be performed, particularly focusing on long-term effects and new information that could be gained with scientific and technological advances.<sup>190</sup>

After the enactment of the Food Additives Amendment, FDA declared saccharin to be GRAS, thereby exempting it from the food additive review process.<sup>191</sup> After tests

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<sup>186</sup> DEPARTMENT OF AGRICULTURE, SACCHARIN IN FOOD, FOOD INSPECTION DECISION 142 (1912).

<sup>187</sup> *Id.*

<sup>188</sup> See 42 Fed. Reg. 19996 (1977).

<sup>189</sup> NATIONAL ACADEMY OF SCIENCES, THE SAFETY OF ARTIFICIAL SWEETENERS FOR USE IN FOODS 7 (1955).

<sup>190</sup> *Id.* at 8.

<sup>191</sup> *Saccharin: A Case Study*, *supra* note 180, at 29.



showing that a mixture of saccharin and cyclamate led to increased incidence of bladder tumors in laboratory rats, FDA, believing cyclamate to be the responsible substance, removed only cyclamate from its GRAS list in October 1969,<sup>192</sup> allowing saccharin to retain its GRAS status. Removing cyclamate's GRAS status led, as discussed earlier, to an effective ban of cyclamate, which had several consequences: it led the public to realize, for the first time, that commonly used food additives may be unsafe; this realization in turn caused an increased level of food safety regulation.<sup>193</sup> Cyclamate's GRAS revocation and the resulting effective ban (and public panic) also led to FDA's decision to create a middle ground between a substance having GRAS status and being banned: the interim food additive category.<sup>194</sup> Further, because the effective ban of cyclamate left saccharin as the only approved artificial sweetener, it led FDA to try further to determine whether saccharin is a safe substance to consume. FDA both asked for another study by the National Academy of Sciences and performed its own in-house chronic feeding study regarding saccharin's safety; the sugar industry also performed a separate chronic feeding study of saccharin in Wisconsin Alumni Research Foundation laboratories.<sup>195</sup>

The report by the National Academy of Sciences declared current levels of saccharin consumption to be safe but, because levels of consumption likely would increase in the future, recommended long-term studies in at least two species; this recommendation would be fulfilled by the studies performed by FDA and Wisconsin

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<sup>192</sup> 34 Fed. Reg. 17063, 17064 (1969).

<sup>193</sup> *Saccharin: A Case Study*, *supra* note 180, at 30.

<sup>194</sup> 21 C.F.R. Part 180 (1983).

<sup>195</sup> 42 Fed. Reg. 19996, 19999 (1977).

Alumni Research Foundation.<sup>196</sup> FDA proposed in 1971 to remove saccharin's GRAS status but to permit it to be used as an interim food additive (thereby avoiding the effective ban that resulted with the removal of cyclamate's GRAS status), with specified acceptable uses and levels, and a with a requirement that products containing saccharin bear a label stating the amount of the sweetener the product contained.<sup>197</sup> At approximately the same time, FDA referred to a study in which saccharin-containing cholesterol pellets caused an increased incidence of bladder tumors in laboratory rats, declaring that the potential carcinogenicity of saccharin needed to be further examined in chronic feeding studies.<sup>198</sup>

The interim food additive regulation for saccharin was promulgated February 1, 1971.<sup>199</sup> By this time, FDA had become aware of the fact that some of the laboratory animals in the highest dose group of the study by the Wisconsin Alumni Research Foundation had, in fact, developed bladder tumors.<sup>200</sup> This dose group, however, consumed enough saccharin to constitute five percent of their daily diet, which was roughly one hundred times the maximum exposure permitted by the interim food additive regulation; FDA declared the amount of saccharin the animals consumed to be the equivalent of a human consuming 875 bottles of diet soda each day.<sup>201</sup> The final results of the Wisconsin Alumni Research Foundation study and of FDA's own study both confirmed the increased occurrence of bladder tumors in male rats.<sup>202</sup>

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<sup>196</sup> NATIONAL ACADEMY OF SCIENCES, SAFETY OF SACCHARIN FOR USE IN FOODS 11 (1970); 42 Fed. Reg. 19999 (1977).

<sup>197</sup> 36 Fed. Reg. 12109, 12110 (1971).

<sup>198</sup> *FDA Fact Sheet: Saccharin* (1971).

<sup>199</sup> 37 Fed. Reg. 2437 (1972).

<sup>200</sup> *Saccharin: A Case Study*, *supra* note 180, at 33.

<sup>201</sup> *Id.* at 33–34.

<sup>202</sup> *Id.* at 35.

FDA then asked the National Academy of Sciences again to review the studies, in hopes of obtaining accurate information on saccharin's safety before its interim food additive regulation was set to expire on June 30, 1973.<sup>203</sup> Several complications, including other studies already underway and questions regarding the accuracy of the completed studies, prevented the timely decision, causing FDA to extend the interim food additive regulation.<sup>204</sup> FDA also stated that other "toxicity factors" that occurred only at extremely high doses of saccharin, such as high urinary concentrations of sodium, depressed weight gain, decreased survival and weight of the pups at weaning, or possible bladder stones and irritation, may be responsible for the bladder tumors in the high-dose group.<sup>205</sup>

The National Academy of Sciences issued its report, which focused primarily on saccharin's possible carcinogenicity, in December 1974.<sup>206</sup> The report declared that saccharin's safety could not be determined simply by its causation (or lack thereof) of tumors in laboratory animals; instead, such a determination must consider all possible factors that could cause the bladder tumors before determining whether saccharin is safe for human consumption.<sup>207</sup>

Only two of the eleven feeding studies that were conducted regarding saccharin (those completed by FDA and Wisconsin Alumni Research Foundation) showed possible carcinogenicity; these two studies were completed expressly for such a purpose and differed from others in that they involved two generations of laboratory animals (to

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<sup>203</sup> *Id.*

<sup>204</sup> 38 Fed. Reg. 13733 (1973).

<sup>205</sup> *Id.* at 13734.

<sup>206</sup> NATIONAL ACADEMY OF SCIENCES, SAFETY OF SACCHARIN AND SODIUM SACCHARIN IN THE HUMAN DIET (1974).

<sup>207</sup> *Id.* at 6.

account for possible consumption of saccharin by pregnant women).<sup>208</sup> The National Academy of Sciences declared the increased incidence of bladder tumors in FDA's study to be statistically significant, but stated that the similar result in Wisconsin Alumni Research Foundation's study was merely of questionable statistical significance.<sup>209</sup> The Academy concluded, however, that the studies had not established conclusively that saccharin was (or was not) carcinogenic, primarily because the studies failed to clarify whether saccharin itself resulted in the increased incidence of tumors or if, instead, the tumors resulted from impurities in the studies.<sup>210</sup> The Academy then recommended extensive additional studies, requiring FDA to further defer final determination of saccharin's safety.<sup>211</sup>

In January 1975, Senator Gaylord Nelson asked the General Accounting Office to investigate and report on FDA's handling of the saccharin situation.<sup>212</sup> The General Accounting Office issued its report on August 16, 1976, giving saccharin a less-than-clean bill of health.<sup>213</sup> Because of the serious questions of saccharin's safety that were being examined at that time, the General Accounting Office questioned FDA's justification of continuing to permit its use; the report noted that even some FDA scientists were skeptical about discounting the results of tests showing potential carcinogenicity.<sup>214</sup> The report concluded that a substance such as saccharin could expose the public to unnecessary risk and recommended that the Secretary of the Department of Health, Education, and Welfare direct FDA to reconsider its justification for continuing

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<sup>208</sup> *Saccharin: A Case Study*, *supra* note 180, at 37–38.

<sup>209</sup> *Safety of Saccharin*, *supra* note 206, at 50.

<sup>210</sup> *Id.* at 63.

<sup>211</sup> *Id.* at 63–64.

<sup>212</sup> See General Accounting Office, “Need to Resolve Safety Questions on Saccharin,” HRD 76-156 (1976).

<sup>213</sup> *Id.*

<sup>214</sup> *Id.* at 11–12.

to permit marketing of saccharin and to consider either banning it or issuing a permanent food additive regulation.<sup>215</sup>

After he left office, the FDA Commissioner who refused to ban saccharin, Dr. Charles Edwards, stated

Technically, I could have banned saccharin immediately under the Delaney Clause, in early 1972, on the basis of those animal studies. I did not take that step because, once again, it was clear to me that the law should not be interpreted to yield absurd results. Saccharin was, at that time, the only remaining nonnutritive sweetener on the market. American consumers demand the availability of diet food products. It is irrelevant whether these diet products produce quantifiable health benefits or whether consumers simply like them. The point is that saccharin, like nitrite and many other important food substances, has come to be accepted and expected by the American public, and any law which does not recognize this simply will not work.<sup>216</sup>

Thus, Dr. Edwards candidly admitted that saccharin's actual health risks would have warranted a ban, but the major reason for refusing to allow such a ban was the lack of any remaining artificial sweetener that would result.

Beginning in fall of 1976, FDA drafted two notices,<sup>217</sup> one of which further extended saccharin's interim food additive regulation, noting FDA's concern about saccharin's safety and its intention to reach a final decision about whether the sweetener

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<sup>215</sup> *Id.* at 27.

<sup>216</sup> "Oversight of Food Safety, 1983," Hearings before the Senate Comm. on Labor and Human Resources, 98th Cong., 1st Sess. 20–21 (1983).

<sup>217</sup> 42 Fed. Reg. 1461 (1977).

could be marketed; the notice was published in the *Federal Register* on January 7, 1977.<sup>218</sup> In particular, FDA noted that it expected a final decision shortly after the conclusion of the Canadian study, the results of which were expected to be available in January 1978.<sup>219</sup> FDA continued to permit marketing of saccharin in the interim period, however, declaring its belief that such a decision would not significantly increase the risk of harm to the public, yet affirming that it would be willing even to ban saccharin (and quickly) if it became necessary to do so.<sup>220</sup>

The day before the notice was published, the reporter Jack Anderson published a column asserting that FDA had and was concealing evidence of saccharin's carcinogenicity and that many FDA officials believed the sweetener should be banned.<sup>221</sup> Indeed, the two-generation feeding study, which addressed many of the uncertainties that had been present in earlier feeding studies, confirmed the existence of a significant increase in bladder tumors in the rats that had been fed saccharin.<sup>222</sup>

On March 9, 1977, the day after FDA and Canadian officials reviewed results of the study, both nations took steps to ban saccharin; in Canada, the sweetener's use would be forbidden in soft drinks beginning July of that year, while, in the United States, FDA announced its plans for prompt rulemaking proceedings to withdraw its approval of saccharin.<sup>223</sup>

FDA was left with a dilemma: it now had no doubt that saccharin was at least somewhat carcinogenic, but had several problems with implementing a ban. The agency

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<sup>218</sup> *Id.*

<sup>219</sup> *Id.*

<sup>220</sup> *Id.*

<sup>221</sup> Anderson, *FDA Sits on Saccharin-Cancer Data*, THE WASHINGTON POST, Jan. 6, 1977, at D.C. 9.

<sup>222</sup> See 42 Fed. Reg. 19996, 20000 (1977).

<sup>223</sup> *Saccharin: A Case Study*, *supra* note 180, at 47.

did not want to panic the public (hence, it did not wish to recall saccharin-containing products, particularly because it believed they would be the cause of no immediate danger to the public) and also faced the difficulty of having no alternative available sugar substitute (unlike Canada, which had not banned cyclamate).<sup>224</sup> Thus, the press release announcing FDA's decision to ban the substance based on the Delaney Clause and the Canadian study noted saccharin's potential carcinogenicity, yet stressed the lack of an immediate hazard or need for a recall of saccharin-containing products (with the press release including, *inter alia*, the statistic of needing to drink roughly eight hundred diet sodas each day for harm to result).<sup>225</sup>

After FDA's announcement, some criticized the agency for banning saccharin without certainty of whether it was, in fact, carcinogenic; the critics used the eight hundred-cans-of-soda statistic discussed earlier and the uncertainty of the reliability with which high-dose animal studies apply to humans as evidence for their assertions.<sup>226</sup> The fact that FDA declared its reason for the ban to be that the law required it rather than because of affirmative proof that saccharin does cause cancer merely added to the critics' arguments.<sup>227</sup> This backlash led to calls for congressional hearings to review FDA's decision.<sup>228</sup>

FDA's response came on April 15, 1977 in its formal proposal for a ban.<sup>229</sup> The proposal discussed saccharin's history, the scientific basis for its ban, the appropriateness of high-dose animal studies, and a quantitative risk assessment of saccharin to humans.<sup>230</sup>

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<sup>224</sup> *Id.*

<sup>225</sup> *Id.* at 47–48.

<sup>226</sup> *Id.* at 49.

<sup>227</sup> *Id.*

<sup>228</sup> *Id.*

<sup>229</sup> 42 Fed. Reg. 19996 (1977).

<sup>230</sup> *Id.* at 19997–19998.

FDA declared the maximum risk of developing bladder cancer as a result of drinking one diet soda each day to be four in ten thousand; the risk could be nonexistent, but the maximum risk, if everyone in the United States at the time the quantitative risk assessment was performed drank one diet soda each day, could result in 1200 additional cases of bladder cancer annually.<sup>231</sup> Although available epidemiological data showed the existence of no connection between saccharin consumption and an increase in the chances of developing bladder cancer, FDA stressed that human studies normally are not able to detect small increases in such a risk.<sup>232</sup> The agency also reiterated the requirement that saccharin be banned under the Delaney Clause because of its potential carcinogenicity.<sup>233</sup>

In response to assertions by diabetics that saccharin was necessary for therapeutic use, FDA only allowed the possibility of using it for such purposes for drugs, not for any foods.<sup>234</sup> FDA declared that it would be strict in allowing the use of saccharin in drugs, however; the only way the sweetener would be permissible would be if it were essential to keeping a drug product palatable (to the extent that the relevant population would be unlikely to consume the drug product without the added palatability provided by saccharin) and the benefit of using saccharin thereby outweighed the risk.<sup>235</sup> FDA also noted the potential use of saccharin as a drug in tablet, powder, or liquid form if it were clinically proven that the substance had genuine therapeutic benefits for diabetics or obese persons if it were accompanied by a warning of its potential carcinogenicity;<sup>236</sup>

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<sup>231</sup> *Id.* at 20000–20002.

<sup>232</sup> *Id.*

<sup>233</sup> *Id.* at 20002.

<sup>234</sup> *Id.* at 20002–05.

<sup>235</sup> *Id.*

<sup>236</sup> *Id.*



whether FDA genuinely believed such a use to be possible seems quite doubtful, however, particularly because of the demanding standards the law has for proving a drug's effectiveness.<sup>237</sup>

### iii. Political controversy

FDA's decision to ban saccharin became highly politically controversial. The Senate Human Resources Committee requested the Office of Technology Assessment to prepare a report on methods of testing for carcinogenicity, saccharin's risks and benefits, and potential alternative artificial sweeteners; a draft report endorsed the usage of animal testing, though it noted resulting uncertainties when extrapolating the data to humans; the conclusion was that saccharin indeed is carcinogenic, although its carcinogenicity to humans remained uncertain.<sup>238</sup> Though the report noted that using saccharin may indeed have benefits, particularly to diabetics and overweight individuals, it concluded that no valid tests confirmed these benefits.<sup>239</sup> The report did not predict the date of available alternative sugar substitutes.<sup>240</sup>

Soon after, the National Cancer Institute of Canada released the results of a study asserting the existence of a positive association between use of saccharin and bladder cancer in human males; according to their data, the use of saccharin made males 1.6 times more likely to develop bladder cancer, though no similar association was shown in females.<sup>241</sup>

Congress remained quite strongly in favor of delaying the ban on saccharin for several reasons. Many believed that the evidence showing that the sweetener was

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<sup>237</sup> See *id.* at 20003–05.

<sup>238</sup> OFFICE OF TECHNOLOGY ASSESSMENT, *CANCER TESTING TECHNOLOGY AND SACCHARIN 5* (1977).

<sup>239</sup> *Id.* at 6.

<sup>240</sup> *Id.* at 41–45.

<sup>241</sup> *Saccharin: A Case Study*, *supra* note 180, at 54.

actually carcinogenic in humans, or that its risks to humans outweighed its benefits, was uncertain; thus, they believed that consumers should have the freedom to determine whether to purchase and consume saccharin and saccharin-containing products given their own particular life and health factors (particularly their weight and diabetic status).<sup>242</sup>

Therefore, Senator Edward Kennedy and Congressman Paul Rogers, the committee chairmen, each wrote a bill proposing both a delay on FDA action and further study by an outside group (preferably the often-utilized National Academy of Sciences) of the scientific and policy issues in question.<sup>243</sup> Senator Kennedy's proposal was significantly more strict about warnings than that of Congressman Rogers, however: it would mandate posted warnings in places selling saccharin or saccharin-containing products (as would the Rogers bill) as well as warnings on product labels and all advertisements for saccharin-containing products (which the Rogers bill would not require).<sup>244</sup>

Senator Edward Kennedy eventually believed congressional action to be inevitable, concluding that saccharin indeed was harmful to the public health and that Congress needed to minimize the risk of harm resulting from involuntary exposure to saccharin.<sup>245</sup>

The Senate's version ultimately prevailed and was signed into law on November 23, 1977, becoming known as the Saccharin Study and Labeling Act (SSLA).<sup>246</sup> The SSLA postponed FDA action for eighteen months, directed the Secretary of the

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<sup>242</sup> *Id.* at 6–7.

<sup>243</sup> *Saccharin: A Case Study*, *supra* note 180, at 54–55.

<sup>244</sup> *Id.* at 55.

<sup>245</sup> *Id.* at 56.

<sup>246</sup> *Id.* at 57.

Department of Health, Education, and Welfare to arrange for two new studies by the National Academy of Sciences (one to study specific scientific issues, including risks and benefits, and one to study the scientific and policy issues that occur in the regulation of all carcinogenic and otherwise toxic food substances), and required specific warning labels to appear on all saccharin-containing products.<sup>247</sup>

As the information on the history of regulation of saccharin reveals, FDA's decisions are not always based simply on research, science, and statistics. Now, certain interest groups have caused the agency's decisions to be peppered with a degree of politicization. Many supporters of the Delaney Clause likely would argue this to be a negative development: FDA, they would argue, should stick to the facts of a substance's potential dangers and keep politics out of their decision. After all, the politicization of saccharin's approval may leave FDA less likely to declare a substance unsafe, even in the face of uncontroverted scientific evidence showing it to be marginally so, if it is a substance the agency fears will have many powerful supporters fighting for it to remain on the market. However, though sheer politicization is unlikely to be considered good by anyone, those who support allowing public consumption of substances such as saccharin may be responsible for enlightening the public to contrary evidence, which shows the substance's safety, that FDA may gloss over in hopes of an uncontroversial ban. The politicization, at least, may give the public more complete information about questionable substances.

#### C. Carcinogens resulting from cooking methods

Cooking and preservation methods, even traditionally used ones, as FDA scientists have stated, frequently contaminate otherwise innocuous foods with

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<sup>247</sup> *Id.*

carcinogens.<sup>248</sup> Charbroiling and smoking have been known to contaminate the cooked food by the addition of polynuclear aromatic hydrocarbons; pickling contaminates the food with nitrosamines.<sup>249</sup> Far more such examples exist, but have been ignored for purposes of FDA regulation under the Delaney Clause because such exposure to carcinogens is nearly omnipresent and would be almost impossible to control and regulate.<sup>250</sup>

#### D. Other carcinogens

Although most sugar substitutes (as the previous discussion indicates), and other food additives, undergo rigorous testing before being permitted for sale on the market, and often even after their approval, to ensure that they are not carcinogenic, many commonly-ingested foods and beverages either are or contain carcinogens. This is unpleasant news to many (albeit perhaps slightly naïve) individuals who believe that, if a product is permissible to sell, it cannot possibly be harmful to consume. In fact, one of the nation's most cherished beverages, coffee, has been reported to contain over one thousand chemicals; twenty-eight of these chemicals have been tested, and nineteen of the twenty-eight are rodent carcinogens.

Coffee, however, is far from the only commonly-eaten food or beverage containing carcinogenic ingredients. Such ingredients appear in numerous products that FDA would be highly unlikely ever to ban or even strictly regulate, realizing both the dangers of political backlash and sheer improbability of such action.

FDA does not always refrain from regulating natural foods. By 1954, the agency had banned the use of natural tonka beans as food because a constituent of the beans,

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<sup>248</sup> FOOD AND DRUG LAW, *supra* note 3, at 1174.

<sup>249</sup> *Id.*

<sup>250</sup> *Id.*

coumarin, had been determined carcinogenic.<sup>251</sup> In 1960, FDA banned the use of safrole and oil of sassafras due to potential carcinogenicity; the ban in 1973 was extended to include natural sassafras bark for making sassafras tea.<sup>252</sup> Following this, however, FDA has not attempted to ban natural food products with carcinogenic constituents, though the agency maintains the official position that a substance that is found to be carcinogenic in animals can never be considered GRAS (although a substance with a carcinogenic constituent may be).<sup>253</sup>

Acetaldehyde, which naturally occurs in coffee and ripe tart fruits, and also is a product of oxidation of ethanol, is a probable human carcinogen.<sup>254</sup> Acrylamide occurs in cooked starchy foods (e.g., French fries, potato chips, heated bread); it also can be found in prunes, olives, and dried pears, as well as certain beverages (most notably coffee and prune juice).<sup>255</sup> Safrole is a liquid that typically is extracted from the root-bark or the fruit of the sassafras plant in the form of sassafras oil; it also may be synthesized from additional compounds. It is found naturally in numerous plants and spices (e.g., basil, black pepper, nutmeg, and cinnamon). The United States government regards safrole as a weak carcinogen in rats.

Many commonly eaten foods also contain human mutagens. Mutagens are substances, either natural or manufactured, that change human DNA, increasing the frequency of mutations. Although many of these mutations are harmless, producing no noticeable effect, or even (on rare occasions) producing beneficial effects, some

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<sup>251</sup> *Id.* at 1175.

<sup>252</sup> *Id.*

<sup>253</sup> *Id.*

<sup>254</sup> *Chemical Summary for Acetaldehyde*, ENVIRONMENTAL PROTECTION AGENCY, [http://www.epa.gov/chemfact/s\\_acetal.txt](http://www.epa.gov/chemfact/s_acetal.txt) (last visited February 2011).

<sup>255</sup> *Survey Data on Acrylamide in Food: Individual Food Products*, FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/ChemicalContaminants/Acrylamide/ucm053549.htm> (last visited February 2011).

mutations can be quite dangerous, even lethal, rendering mutagens a category of which people are wary. Though mutagens are not themselves regulated under the Delaney Clause, mutagenicity and carcinogenicity often are strongly correlated. Mutagenesis may lead to carcinogenic tumor development.

The American Council on Science and Health listed the carcinogens that are naturally present in many commonly-eaten holiday foods. The list likely would surprise much of the public, many of whom likely would believe a significant number, perhaps even most, of the foods on the list to be safe, or at least not affirmatively harmful, for public consumption.

Vegetables often contain mutagenic or carcinogenic (or potentially carcinogenic) ingredients. For example, in carrots, one will find both aniline and caffeic acid.<sup>256</sup> Aniline is a rodent carcinogen; however, the information concerning the carcinogenicity of aniline is contradictory and the International Agency for Research on Cancer has listed it as not classifiable as to its carcinogenicity to humans; early linkage to bladder cancer now has been attributed to other substances. Caffeic acid also is a rodent carcinogen, still listed as such because of the results of two early studies on rodents. Tomatoes contain benzaldehyde (which is a rodent carcinogen), caffeic acid, hydrogen peroxide (which is a mutagen and rodent carcinogen), and quercetin glycosides (which are mutagens and rodent carcinogens).<sup>257</sup> Celery contains caffeic acid, furan derivatives (which are mutagens), and psoralens (which are mutagens and both rodent and human carcinogens).<sup>258</sup> Broccoli spears contain allyl isothiocyanate (which is a mutagen and

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<sup>256</sup> ACSH HOLIDAY DINNER MENU, *American Council on Science and Health*, [http://www.acsh.org/publications/pubID.103/pub\\_detail.asp](http://www.acsh.org/publications/pubID.103/pub_detail.asp) (last visited February 2011).

<sup>257</sup> *Id.*

<sup>258</sup> *Id.*

rodent carcinogen).<sup>259</sup> Baked potatoes contain ethyl alcohol (which is a rodent and human carcinogen) and caffeic acid, and sweet potatoes contain ethyl alcohol and furfural (which is a mutagen and rodent carcinogen).<sup>260</sup>

Fruits are not immune from potential carcinogenicity either: a fruit tray composed of apples, grapes, mangos, pears, and pineapple would contain numerous carcinogens. For example, apples contain acetaldehyde, which is a mutagen and rodent carcinogen and also a probable human carcinogen<sup>261</sup> and, according to a 2009 report by the International Agency for Research on Cancer, a Group 1 human carcinogen. Apples also contain benzaldehyde, quercetin glycosides, and estragole, which is a rodent carcinogen.<sup>262</sup> Apples, grapes, and mangos all contain caffeic acid.<sup>263</sup> Mangos contain d-limonene, which is a rodent carcinogen and also is listed as not classifiable as to its carcinogenicity to humans, but as having sufficient evidence to support its carcinogenicity in laboratory animals, by the International Agency for Research on Cancer;<sup>264</sup> the Carcinogenic Potency Project has estimated that d-limonene causes cancer at a rate approximately equivalent to that caused by caffeic acid.<sup>265</sup> Pineapple contains ethyl acrylate, which is also a rodent carcinogen.<sup>266</sup>

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<sup>259</sup> *Id.*

<sup>260</sup> *Id.*

<sup>261</sup> *Chemical Summary for Acetaldehyde*, *supra* note 254.

<sup>262</sup> *ACSH Holiday Dinner Menu*, *supra* note 256.

<sup>263</sup> *Id.*

<sup>264</sup> International Agency for Research on Cancer, d-limonene, <http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-16.pdf> at 322.

<sup>265</sup> *Ranking Possible Cancer Hazards from Rodent Carcinogens, Using the Human Exposure/Rodent Potency Index (HERP)*, CARCINOGENIC POTENCY PROJECT, <http://potency.lbl.gov/pdfs/herp.pdf> (last visited March 2011).

<sup>266</sup> *ACSH Holiday Dinner Menu*, *supra* note 256.

Mixed roasted nuts contain aflatoxin (which is a mutagen and both a human and a rodent carcinogen) and furfural.<sup>267</sup> Roast turkey and roast beef contain heterocyclic amines, which are mutagens and rodent carcinogens caused from cooking certain meats at high temperatures, and cranberry sauce contains furan derivatives.<sup>268</sup> Rolls with butter would contain acetaldehyde, ethyl alcohol, benzopyrene (which is a mutagen and rodent carcinogen that is considered to be a possible cause of lung cancer), ethyl carbamate, furan derivatives, furfural, and benzene.<sup>269</sup> Benzene is a rodent carcinogen that is found in butter.<sup>270</sup> It is also classified as a human carcinogen by the United States Department of Health and Human Services; long-term exposure to benzene undisputedly may lead to the development of leukemia.<sup>271</sup>

Holiday desserts may contain carcinogens as well. Pumpkin pie contains benzopyrene, coumarin, methyl eugenol, and safrole.<sup>272</sup> Coumarin is a rodent carcinogen that is found in cinnamon; methyl eugenol is a rodent carcinogen found in both cinnamon and nutmeg, and safrole, as mentioned earlier, is a rodent carcinogen that is found in nutmeg and black pepper; its risk of carcinogenicity is considered roughly equivalent to that of limonene and caffeic acid.<sup>273</sup> Apple pie, furthermore contains acetaldehyde, caffeic acid, coumarin, estragole, ethyl alcohol, methyl eugenol, quercetin glycosides,

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<sup>267</sup> *Id.*

<sup>268</sup> *Id.*

<sup>269</sup> *ACSH Holiday Dinner Menu*, *supra* note 256.

<sup>270</sup> *Id.*

<sup>271</sup> *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs*, WORLD HEALTH ORGANIZATION INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, <http://monographs.iarc.fr/ENG/Monographs/suppl7/suppl7.pdf>, at 59 (last visited March 2011).

<sup>272</sup> *Id.*

<sup>273</sup> *Ranking Possible Cancer Hazards from Rodent Carcinogens, Using the Human Exposure/Rodent Potency Index (HERP)*, *supra* note 265.



and safrole.<sup>274</sup> As discussed earlier in the fruit section, apples are responsible for the acetaldehyde, caffeic acid, estragole, and quercetin glycosides.

Beverages, likewise, are not always quite as innocuous as many consumers might imagine or wish them to be. As already mentioned, coffee is filled with potential carcinogens. Wine contains ethyl alcohol and ethyl carbamate.<sup>275</sup> Tea contains benzopyrene and quercetin glycosides.<sup>276</sup> Jasmine tea contains benzyl acetate (which is a rodent carcinogen).<sup>277</sup>

#### IV. Contradictions

FDA's regulations under the Delaney Clause have resulted in several contradictory rulings. The rest of this paper will examine whether such contradictions are avoidable and, if they are not, whether they are the lesser evil as compared to FDA's alternative possibilities.

##### A. Artificial sweeteners

One major contradiction is between artificial sweeteners. As discussed earlier, cyclamate was banned fairly quickly, and with relatively little controversy, on less-than-certain evidence of its carcinogenicity. Similar (and arguably far stronger) evidence of saccharin's carcinogenicity, though triggering a great deal of concern and controversy, did not result in a ban.

A good reason for the stronger resistance to banning saccharin is that, at the time that the ban would have occurred, it would have left the United States with no approved artificial sweetener on the market. For many, particularly diabetic and obese consumers,

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<sup>274</sup> *Id.*

<sup>275</sup> *Id.*

<sup>276</sup> *Id.*

<sup>277</sup> *Id.*

this possibility became quite alarming. Now, however, many additional sugar substitutes are available. Some may assert that, with their developments, FDA should rethink banning saccharin.

However, one must consider whether the real problem was FDA's decision not to ban saccharin or its decision to ban cyclamate on uncertain evidence. The quick ban of cyclamate left FDA with a precedent that was effectively impossible to follow consistently. As noted earlier, the *de minimis* exception to the Delaney Clause recognizes that scientific development has rendered it difficult not to detect some miniscule potential carcinogenic effect in almost any food.

#### B. Food additives v whole foods

As discussed, many natural foods, such as fruits, vegetables, and spices, contain carcinogenic or mutagenic substances. These substances are not chemicals added by humans to the foods and, for the most part, would not be declared "added" even under FDA's definition of the term; the carcinogens are naturally present. However, were FDA to begin dictating to the public exactly how many apples they were allowed to consume daily, it is safe to say that a backlash would follow (and would do so rather quickly). This is the case even though the vast majority of consumers know little, and in many cases nothing, of the potential carcinogens or mutagens present in the foods they purchase. Why, then, does FDA have the right (and, according to many, the obligation) to regulate (either through forbidding the purchase, limiting the amount that the public should consume, or requiring explicit and detailed warning labels) the ability of United States consumers to purchase and consume products containing carcinogens that are not

naturally present in the food, even though the danger may be no greater, and in some cases significantly less, than that posed by many fruits and vegetables?

In some cases, of course, the natural foods may be so slightly carcinogenic that they would fall under the *de minimis* exception. The primary inconsistency involves the natural foods that are carcinogenic to a level that precludes their falling under such an exception. Much of the problem here, of course, stems from the Delaney Clause's regulation of food *additives*, not foods themselves.

So does the Clause actually provide a meaningful solution to the problem of carcinogenicity in foods? Some say yes, because the Clause undoubtedly reduces some incidences of cancer caused by carcinogenic food ingredients. This cannot be denied: even if the Clause is not perfect in its application, it does at least remove some carcinogens and carcinogenic-containing food substances from the market. Others, however, may argue that the Clause is more problematic than helpful, particularly because it manages to be simultaneously overreaching and underreaching: it leads to bans of certain food additives of which only negligible evidence of carcinogenicity exists, even though the tests are imperfect and not all the products actually may be carcinogenic; it also fails to ban certain products (whole foods and additives perhaps improperly declared to be GRAS) that may be at least as carcinogenic as many of the banned products under the Delaney Clause.

Even though the Clause regulates food additives, however, and, as noted earlier, FDA takes an expansive view on what is considered an additive for purposes of regulation, FDA has not regulated the carcinogens resulting from traditional cooking or preserving techniques. Understandably, such regulation would be prohibitively difficult;

however, in light of the Agency's decision not to regulate such carcinogenic food additives, the strict regulation of other forms of potentially carcinogenic food additives seems somewhat perplexing.

Further problematic is the fact that FDA initially nearly constantly interpreted the Food and Color Additive Amendments to ban the use of any additive that definitely or even allegedly contained even small amounts of carcinogenic chemicals, even when the additive itself had not been found to be carcinogenic.<sup>278</sup> The agency eventually began to use what it called the constituents approach, distinguishing between the actual additive and its constituents to determine when the Delaney Clause would be triggered.<sup>279</sup> Thus, although the constituent is part of the additive itself, it would not be considered an additive for purposes of regulation.<sup>280</sup>

FDA's justification for the new approach was due to developments in law and technology as well as the text of the Delaney Clause. Regarding the law, the United States Court of Appeals for the District of Columbia Circuit held in 1979 that there is "administrative discretion, inherent in the statutory scheme, to deal appropriately with *de minimis* situations."<sup>281</sup> Thus, according to FDA, it possessed authority to disregard carcinogenic chemicals in non-carcinogenic additives if tests demonstrate a "reasonable certainty of no harm" that would result from the additive.<sup>282</sup> Regarding technological developments, FDA determined that it was able adequately to assess the upper level of risk (though the actual level of risk remained uncertain at low levels) from using a noncarcinogenic additive with a carcinogenic constituent through the use of

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<sup>278</sup> 47 Fed. Reg. 14464 (1982).

<sup>279</sup> *Id.*

<sup>280</sup> *Id.*

<sup>281</sup> *Monsanto Co. v. Kennedy*, 613 F.2d 947 (D.C. Cir. 1979).

<sup>282</sup> 47 Fed. Reg. 14464 (1982).

extrapolation.<sup>283</sup> Regarding the text of the Delaney Clause itself, the agency noted that it does not force deeming an additive unsafe if the additive or any of its chemical constituents are found to be carcinogenic, but simply if the additive itself were found to be so.<sup>284</sup>

Thus, FDA determined that application of such a procedure would allow nothing but “minor levels of carcinogenic chemicals” to pass its screen due to the low acceptable levels that would result.<sup>285</sup> The United States Court of Appeals for the Sixth Circuit has upheld FDA’s right to make such a determination with regard to color additives, declaring that it “agree[d] with the FDA’s conclusion that since it ‘has discretion to find that low-level migration into food of substances in indirect additives is so insignificant as to present no public health or safety concern ... it can make a similar finding about a carcinogenic constituent or impurity that is present in a color additive.’”<sup>286</sup>

What, then, is the solution to the various inconsistencies? Opinions likely divide between two opposite solutions: desiring FDA to regulate potential carcinogens more strongly and to do so less strongly. The former solution undoubtedly would lead to numerous absurd results: requiring FDA to be internally consistent by regulating all potential carcinogens, whether whole foods or additives, as strongly as its strictest regulation of such a product would lead to the banning of substances such as ethyl alcohol and apples. Even those who think internal consistency by leveling up the amount of regulation to the point of equaling the most strongly-regulated foods or food additives likely would be appalled at this result.

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<sup>283</sup> *Id.*

<sup>284</sup> *Id.* at 1158.

<sup>285</sup> *Id.*

<sup>286</sup> *Scott v. Food and Drug Administration*, 728 F.2d 322 (6th Cir. 1984).

Although the latter solution may lead to problems as well, focusing FDA's role more on providing information rather than regulating and banning carcinogens would be beneficial in many ways. If FDA simply were to perform the necessary tests to determine the potential carcinogenicity of various substances and then to require food products to be labeled and coded according to carcinogenic potential for the general public, and provide more detailed information broken down by age, gender, race, and other factors on a website, the public would have access to information necessary to make an informed decision about which products to consume.

As discussed earlier, this approach would be costly for FDA: its tests would have to be extensive, and its information provision would need to be quite detailed. The agency would avoid many political costs that it currently faces under the Delaney Clause, however, by being the intermediary between warring factions, each of whom is willing to blame FDA if the agency decides against its position. This approach also would avoid placing FDA in as many politically heated situations, allowing the agency to maintain its professionalism without appearing biased.

Further potential objections to this position include the fear that, even if FDA provided complete information of carcinogenic potential, or if the agency required the food manufacturers to do so, a great deal of the public would fail to make a wise choice, and would consume an excessive amount of carcinogenic food. Those arguing this may desire a more paternalistic approach by the government, assuming the public is unable, or unwilling, to make choices for themselves. This leads into the classic philosophical debate: which should prevail between the government attempting to make the best

decision for all its citizens and the individual liberty to determine what will be best for oneself.

How much control can FDA give up and ensure that the public will have access to accurate information about products to consume? In particular, what would happen if FDA were not even to require detailed labeling of carcinogenicity on food products? Some may believe that, without the government forcing such information provision, the public would be left in the blind. However, if FDA were only to make public, for example, that cyclamate has exhibited some potentially carcinogenic tendencies, and not to require cyclamate-containing products to bear a warning of carcinogenic potential (assuming, however, that the product would at least contain the mention of cyclamate in its ingredients), a likely result is that products not containing cyclamate would advertise this proudly on their packaging.

An example of this phenomenon is the current public resistance to products containing monosodium glutamate (MSG) or trans fats. Although FDA has enforced no ban on either of these substances, nor required an enormous warning label on products containing them, products without these additives proudly declare “No MSG!” or “No trans fats added.” Thus, although products containing carcinogenic substances should contain a mention of their presence in the listing of ingredients, and certainly should be penalized for falsely declaring themselves to be free from them, it appears that an explicit warning may not be the only way to inform consumers of the safest products for consumption.

FDA should, however, either maintain or directly oversee the maintenance of a publicly-available website containing information of all potential carcinogens, as well as

the extent to which each may be carcinogenic to specific subgroups of the population.

This information should be stated in sufficiently simple terms to allow even those without a particularly high level of education to be able to understand and meaningfully apply what they have read.

Overall, it appears that FDA would better serve its purpose by refraining from being involved in the politics that have surrounded Delaney Clause regulation, and the paradoxical results stemming therefrom, and instead focusing on determining carcinogenicity of food additives (and of food themselves) and ensuring that the public has adequate access to information of such carcinogenicity. As noted earlier, however, despite the benefits of such an approach, the likelihood that FDA actually will decide to implement such a strategy seems quite small, due to the necessary costs, the general lack of desire for any governmental body to give up some of its control, and the likelihood of severe criticism and a resulting backlash from staunchly pro-regulatory groups and individuals.